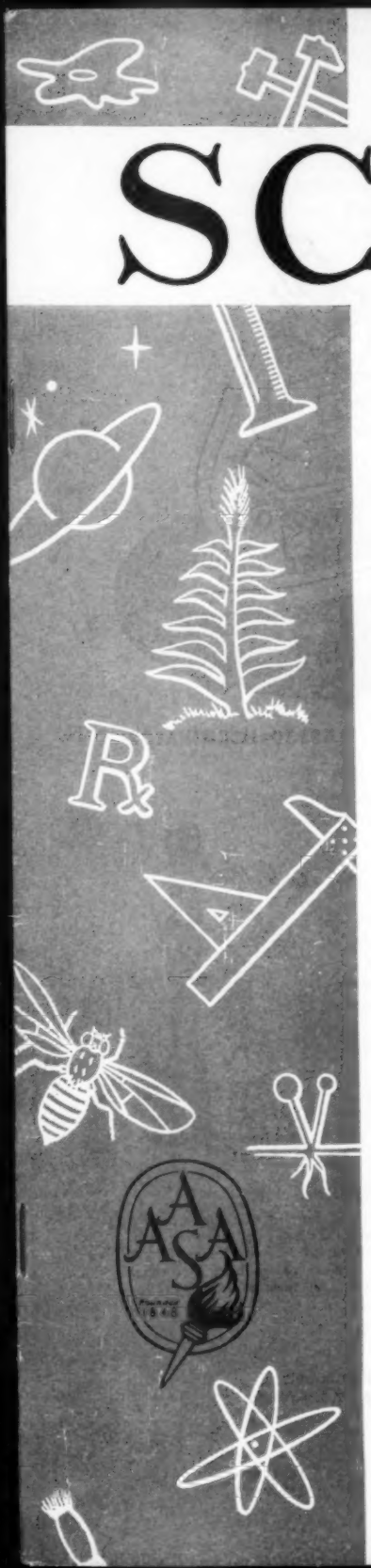

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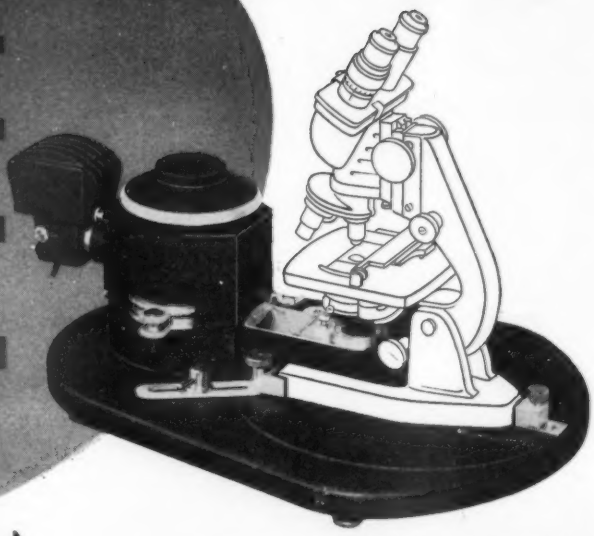

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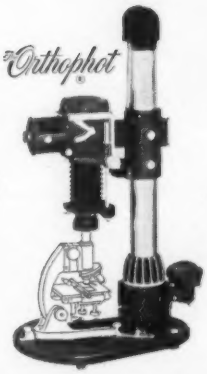

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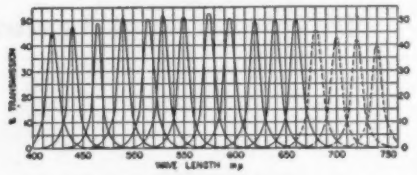

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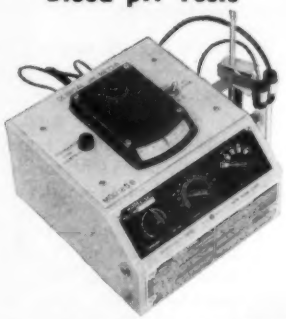

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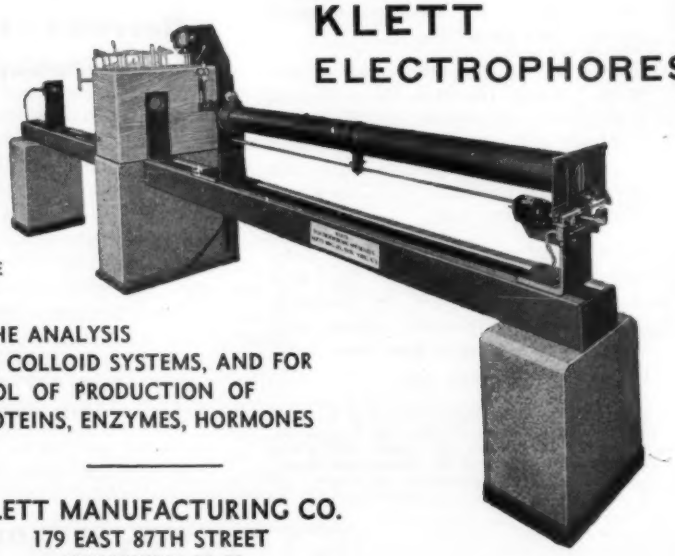

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Berkeley, California, December 26-31, 1954

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The Financing of Medical Schools

BRIAN BIRD [*J. Med. Educ.* 29, No. 6, 35 (June 1954)] points out that deficit financing of medical schools has been an established and accepted fact for many years. Tuition charged to medical students has not paid their educational bill and increasingly pays a smaller part each year. The deficit has thus far been met in state medical schools through government subsidy and in private schools through gifts, endowments and, increasingly, government grants. Since the costs of medical education will probably continue to rise and private sources of funds will probably continue to decrease, it seems likely that eventually only state schools will be able to pay their bills.

As one who believes that the continuation of private medical education is highly desirable, Dr. Bird suggests that the medical profession pay its own way. Tuition cannot be increased sufficiently to meet costs without limiting medical education to the sons of the rich, obviously an undesirable situation. He notes that practicing doctors are among the higher income groups; yet all have received public support amounting to the funds required to defray the cost of their medical education above the tuition paid. He proposes as an alternative that the medical student, as a potential earner, borrow the funds from his school and repay them after graduation.

Dr. Bird believes that this procedure would not drive students away from private schools but that, on the contrary, it would attract the most eager, most self-respecting students. It is his opinion, furthermore, that any plan which would allow the physician the respectability of financing his own education would be a great deterrent to the state control of medicine. Further, the schools would have sufficient funds to pay their faculties proper salaries. Dr. Bird realizes that there are many other arguments on the subject of financing medical schools. He believes, however, that whatever the approach to the problem the one significant question must be kept clearly evident: "Is there any real reason why doctors should not finance their own education?"—W.L.S. JR.

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The Properdin System and Immunity: I. Demonstration and Isolation of a New Serum Protein, Properdin, and Its Role in Immune Phenomena

Louis Pillemer, Livia Blum, Irwin H. Lepow, Oscar A. Ross, Earl W. Todd, and Alastair C. Wardlaw*

Institute of Pathology, Western Reserve University, Cleveland, Ohio

ON the basis of epidemiological and experimental data, immunity has been divided into two general classes—acquired (or artificial) immunity and innate (or natural) immunity. The discovery in serum of specific protective substances, termed antibodies, has increased knowledge about the mechanism of acquired immunity. In conjunction with naturally occurring cellular and humoral constituents of blood, antibodies play a major role in specific acquired immunity. On the other hand, little is known concerning the factors or mechanisms involved in natural immunity. Landsteiner (*1*) states that substances, not identical with but somewhat analogous to specific acquired antibodies, are produced in certain animals without any relationship to prior antigenic stimuli. These normal substances are characterized by their low order of specificity and by their weak union with antigens. The role of complement, C′, and its four components C′1, C′2, C′3, and C′4 (*2*) in natural immunity reactions has also received considerable attention (*1–4*).

In an attempt to isolate one of the components (C′3) of complement, we encountered a new serum protein (*5*), which may be an important factor in natural immunity. This protein, tentatively named *properdin* (*6*), acts only in conjunction with complement and Mg^{++} and participates in such diverse activities as the destruction of bacteria, the neutralization of viruses, and the lysis of certain red cells. Properdin is a normal serum constituent and differs from antibody in many respects, particularly in its lack of specificity and in its exact requirements for its interactions. Investigators (*7*) from several departments of Western Reserve University have collaborated in studying certain activities of properdin. This report gives a brief summary of the various phases of this work (*8*), and more detailed accounts will follow soon.

Demonstration and Isolation of Properdin and Its Reaction with Zymosan

The insoluble residue from yeast cells that have been digested with trypsin and extracted with water and alcohol (*9*) is known as zymosan. Zymosan is composed mainly of carbohydrate and is derived from the yeast cell wall. Treatment of human serum with zymosan at 37°C inactivates selectively the third component (C′3) of complement. Originally, it was thought that this inactivation occurred by the adsorption of C′3 onto zymosan and that this might be a useful method for isolating C′3. However, all attempts to elute C′3 were unsuccessful (*10, 11*). Further studies (*10, 11*) disclosed that the inactivation of C′3 by zymosan was not a simple adsorption but had some of the characteristics of an enzymatic reaction. The loss of C′3 occurred only at temperatures above 20°C, at *p*H near 7, and in the presence of Mg^{++}. On the other hand, there was a stoichiometric relationship between the amount of zymosan added and the amount of C′3 activity that disappeared. The complexity of the system became even more apparent when the reaction was studied at 17°C. At this temperature, zymosan caused no significant inactivation of C′3 or of any other component of complement. Nevertheless, removal of the added zymosan left an altered serum, because incubation with fresh zymosan at 37°C failed to inactivate C′3. When the zymosan was not removed from the serum after the original incubation at 17°C, inactivation of C′3 took place if the temperature was raised to 37°C. The interpretation of these results is presented in Fig. 1.

Zymosan (Z) at 17°C combines with the new factor, properdin (P), to form an insoluble complex (PZ) that is capable of inactivating C′3 at 37°C but not at 17°C. The C′3 in serum that is deficient in properdin (RP) is not altered by zymosan at either temperature but is inactivated upon the addition of *both* properdin and zymosan at 37°C. This difference in the behavior of RP and normal serum is the basis for the present assay of properdin. Thus, one unit of properdin is defined as the smallest amount of sample that, in the presence of zymosan under controlled conditions, reduces the C′3 titer of an RP from an initial value of 120 units/ml to zero. Details of the assay are given in Appendix 1.

The combination of zymosan with properdin proceeds in stoichiometric proportions. It is retarded in a medium with an ionic strength greater than 0.2 and prevented if the ionic strength is raised to 0.4 or

higher. The PZ complex dissociates into its components, properdin and zymosan, in a medium of high ionic strength. The formation and dissociation of the PZ complex provide the basis for a 3000-fold purification of properdin (see Fig. 2 and Appendix 1).

The inactivation of C'3 by zymosan occurs in two stages. The first stage is the combination of properdin with zymosan to give a PZ complex. This reaction proceeds only at temperatures above 10°C and goes to completion at or above 15°C. The *p*H optimum is close to 7. The complex fails to form in serum treated with cation exchange resin. The missing factor appears to be Mg^{++}, because an effective system can be reconstituted by the addition of Mg^{++} to 5×10^{-5} *M*. The formation of PZ also requires the presence of factors that resemble components of complement and that are probably identical with them. A variety of conditions known to destroy or to "fix" complement also prevent the formation of PZ. PZ is not formed when zymosan is added to serum fractions that lack C'1, C'2, or C'4 (*3, 12*), or to serums that have been treated with antigen-antibody aggregates (complement-fixation) or with trypsin, or to serums that have been heated at 50 to 52°C for 30 min. Addition of fresh complement or of those complement components that are destroyed by these procedures reconstitutes an active system. The formation of PZ does not significantly deplete any component of complement. The same term, *properdin*, has been employed for the factor in serum and also for the protein eluted from PZ. It has been assumed that the properdin molecule undergoes no changes during these reactions, but present evidence is not conclusive.

The second stage, namely the inactivation of C'3 by PZ, requires Mg^{++}, a temperature above 20°C, and a factor present in the serum proteins insoluble at *p*H 5.5 and ionic strength 0.02. The role of this factor and its relationship to C'1 is under investigation.

Our experiments have shown that properdin is not a specific antibody to zymosan. The combination of properdin and zymosan requires accessory factors that are not needed for the combination of a typical antibody with a typical antigen (Table 1). Moreover, when PZ is added to serum, the effects on complement are strikingly different from those seen after the addition of an antigen-antibody aggregate (complement-fixation) (Table 2). Whereas an antigen-antibody aggregate (for example, Anti-SIII–SIII) "fixes" human C'1, C'2, and C'4 at either 1°C or 37°C and does not significantly inactivate C'3, PZ inactivates C'3 specifically and only at a temperature greater than 20°C.

Table 1. A comparison of the factors and conditions required for the combination of (i) human properdin with zymosan and (ii) antibody with antigen.

Human properdin with zymosan requires	Antibody with antigen does not require
Mg^{++} ions	Mg^{++} ions
Complement	Complement
Temp. $>$ 10°C	Temp. $>$ 10°C
*p*H 6.5 to 8.2	*p*H 6.5 to 8.2
$\mu = < 0.4$	$\mu = < 0.4$

Present evidence suggests that C'3 is an enzyme that either combines irreversibly with its substrate, PZ, or is destroyed in the reaction. Thus, C'3 may play the same role in the properdin system as it does in a specific immune system (*13*). In each case, after the "preparation" of the antigen, either by properdin or by antibody and complement, C'3 may exert its lytic or lethal action. The interaction of properdin with bacteria, red cells, and perhaps even with viruses is probably analogous to the interaction of properdin with zymosan. Experiments to test this hypothesis are in progress.

Properdin Content of Serums from Various Species and Human Body Fluids

Table 3 shows that there are differences in the properdin content of serums from different animal

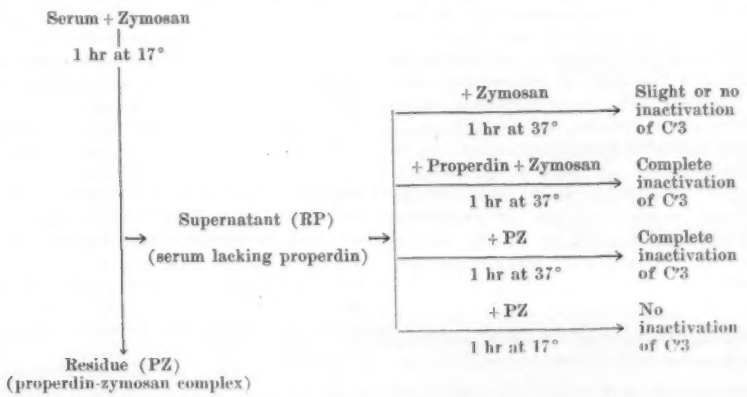

Fig. 1. The combination of zymosan with a substance (properdin) in human serum that is necessary for the inactivation of C'3 by zymosan at 37°C.

Table 2. A comparison of the effect of (i) properdin-zymosan complex (PZ) and (ii) antibody-antigen aggregates (Anti-SIII-SIII) on human complement components.

Human serum and RP treated with	Effect on complement components
PZ for 2 hr at 37°C	Complete loss of C'3; no loss of C'1, C'2, C'4
Anti-SIII-SIII for 2 hr at 37°C	Slight loss of C'3; almost complete loss of C'1, C'2, C'4
PZ for 18 hr at 1°C	No loss of any of the components
Anti-SIII-SIII for 18 hr at 1°C	Slight loss of C'3; almost complete loss of C'1, C'2, C'4

Table 3. Properdin titers in the serums of various animals.

Species	Properdin (units/ml serum)
Rat	25–50
Mouse	10–20
Cow	10–20
Hog	8–12
Human	4– 8
Rabbit	4– 8
Sheep	2– 4
Guinea pig	1– 2

species. Of the warm-blooded animals tested, the rat has the highest titer and the guinea pig has the lowest, while the human is intermediate. These results suggest that properdin may be important in natural immunity, for it is well known that the rat is very resistant to infection and the guinea pig is quite susceptible. Similarly, both the serum properdin level and the natural resistance of the cow and the hog are greater than that of the sheep.

Although normal human serum contains between 4 and 8 units of properdin per milliliter, no properdin is demonstrable in human spinal fluid, ascitic fluid, pleural fluid, colostrum, milk, and extracts of white cells and platelets.

Properties of Human Properdin

Human properdin is a euglobulin with a molecular weight at least 8 times that of gamma globulin. It represents not more than 0.03 percent of the total serum proteins. It is found in serum Fraction III separated by the method of Deutsch *et al.* (*14*). It is precipitated quantitatively with many other euglobulins by dialysis at *p*H 5.5 and low ionic strength. Properdin in serum is stable to heating at 48°C; its activity is slowly destroyed at 50°C, while complete inactivation occurs in 30 min at 56°C. Purified properdin, on the other hand, is stable to heating at 66°C for 30 min (Table 4), but is rapidly inactivated at 100°C. In this respect, properdin resembles certain typical antibodies (*15, 16*) that are more resistant to heat inactivation in the purified state than in serum or on admixture with albumin. Properdin is stable between *p*H 4.8 and 8.4 at ionic strength 0.15 and is not destroyed by freezing and thawing or by prolonged storage at 0°C or −20°C.

Properdin in serum is not destroyed by hydrazine or trypsin or by removal of divalent cations. It is not inactivated or removed by antigen-antibody aggregates. Properdin is not a component of either the clotting or plasmin systems of the blood. Oscar D. Ratnoff (personal communication) found that purified properdin was distinct from fibrinogen, fibrin, prothrombin, thrombin accelerator globulin, convertin, and antihemophilic substance, and from plasminogen, plasmin, and plasmin inhibitors. Properdin is not a component of hemolytic complement and is not necessary in specific immune systems. However, properdin has been found to participate in the bactericidal, virus-neutralizing, and hemolytic activities of serum in the absence of specific antibody but in the presence of complement and Mg^{++}.

The eluate from *bovine* properdin-zymosan complex exhibits properdin and conglutinin (*17, 18*) activities. *Human* properdin, however, has no conglutinating activity. Experiments are in progress to determine whether the conglutinin activity in bovine properdin preparations is due to properdin itself or to an impurity.

Activities of Serum Deficient in Properdin (RP)

Serum deficient in properdin after zymosan treatment (RP) was compared with normal serum in several of the physiological activities of blood. Table 5 shows that the removal of properdin by zymosan at 17°C is a very selective process. RP contains most of the complement and complement component activities of normal serum. The preparation of RP does not destroy factors associated with the clotting or plasmin systems. In fact, RP resembles normal serum in all respects except that (i) it is poorly, or not at all, bactericidal against a variety of organisms, (ii) it has lost its heat-labile virus-neutralizing properties, and (iii) it is not hemolytic against certain red cells.

Table 4. Properties of purified human properdin.

1) Euglobulin with minimum solubility between *p*H 4.8 and 6.5
2) Sedimentation constant about 27 S
3) Represents not more than 2 to 4 μg of protein nitrogen per milliliter of serum, or about 0.03 percent of the serum proteins
4) Stable to heating at 66°C for 30 min
5) Destroyed at 100°C in 5 min
6) Not a component of the blood-clotting, plasmin, or hemolytic complement systems
7) Participates in bactericidal, virus-neutralizing, and hemolytic reactions in the presence of complement and Mg^{++}.

Table 5. Comparison of the factors and activities of untreated human serum and properdin-free serum (RP).

Factor or activity	In untreated serum	In properdin-free serum (RP)
Hemolytic activity for sensitized sheep cells	Present	Present
Individual complement components	Present	Present
Susceptibility to complement fixation	Present	Present
Plasminogen	Present	Present
Plasmin inhibitors	Present	Present
Clotting factors	Present	Present
Hemagglutinin	Present	Present
Susceptibility of C'3 to inactivation by zymosan	Present	Absent
Heat-labile bactericidal activity	Present	Absent
Heat-labile virus-neutralizing activity	Present	Absent
Hemolytic activity for unsensitized cells	Present	Absent

Moreover, as is shown in the following section, the addition of purified properdin to RP restores these activities.

Properdin and Bactericidal Activity

Most of the experiments on the bactericidal activity of human serums were made by using a strain of dysentery bacillus (*Shigella dysenteriae*) as the test organism. The tests were made by adding a known number of viable bacteria, in the form of a washed suspension, to the serum, incubating the mixture for a standard time, and determining the residual number of viable bacteria by serial dilution and plating out. All normal human serums so far tested have shown high bactericidal activity, for they reduced the concentration of viable bacteria by a factor of about 10^5 during 2 to 4 hr incubation at 37°C. There was little variation among individual serums or pools of serums. Control experiments in which bacteria were incubated with buffered albumin solutions showed no reduction in count. In contrast to normal serum, serum from which the properdin had been completely removed (RP) was nonbactericidal, as was properdin by itself. However, RP to which sufficient properdin had been added to give the concentration present in serum had a bactericidal activity almost as high as normal serum. This indicated that properdin, acting in conjunction with factors present in RP, was involved in the bactericidal activity of normal serum against *Sh. dysenteriae*. Present evidence suggests that components of complement are among the necessary factors present in RP. Serum can be rendered nonbactericidal by treatment with reagents known to inactivate complement; for example, antigen-antibody aggregates, low concentrations of hydrazine, and zymosan at 37°C. A systematic study is under way to determine the susceptibility of other bacteria to the properdin system. Preliminary tests with other organisms have also shown that RP is less bactericidal than normal serum.

Properdin and the Heat-Labile Inhibitor of Viral Hemagglutination from Human Serum

Previous investigations (*19*) have demonstrated that human and other serums contain a heat-labile factor that combines with and inactivates viruses. This factor not only inhibits hemagglutination by influenza, mumps, and Newcastle disease viruses but also prevents infection by these agents. Ginsberg and Horsfall (*19*) made a detailed study on this factor in guinea pig serum and showed that hemolytic complement alone was not responsible for such antiviral activities of serum. The present study has been concerned with human serum, but work is in progress on the identification of antiviral factors in other serums, especially guinea pig serum.

In collaboration with Harold Ginsberg, the role of the properdin system in the heat-labile antiviral activity of human serum was investigated. These studies reveal that properdin and serum factors resembling, or identical with, components of complement, especially C'3 and C'4, are necessary for inhibition of viral hemagglutination. The inactivation or removal of any

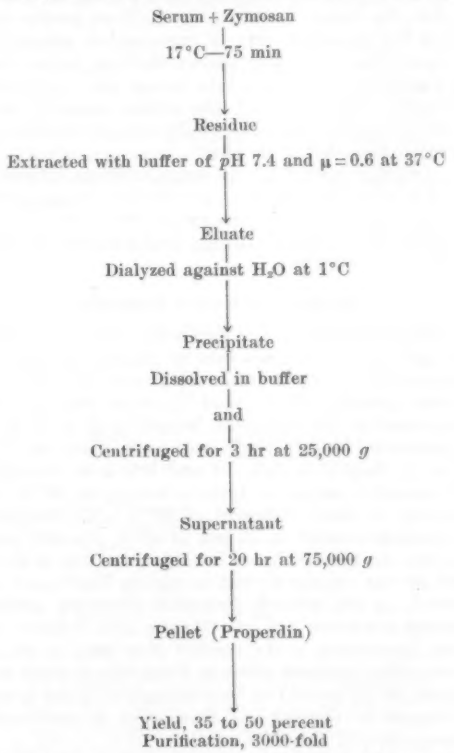

Fig. 2. Flow diagram for the isolation of human or bovine properdin.

Table 6. The properdin and complement titers in rats subjected to total body irradiation of 500 r.

Post-radiation (days)	Properdin (units/ml)	C′ 100% hemolytic units (ml)	Percentage of normal serum values			
			C′1	C′2	C′3	C′4
0	25–35	30–40	100	100	100	100
2	4– 6	50	100	100	100	200
7	< 1	50	100	135	200	200
13	< 1	60	100	200	300	200

of these factors inhibits antiviral activity. The addition of human properdin to serum deficient in properdin (RP) restores its antiviral activity. Studies are in progress to determine the exact role of the properdin system in the neutralization of viruses.

The Properdin System and Total Body Irradiation

Severe bacteremia is commonly encountered following total body irradiation of animals (*20, 21*). Antibiotics given early in the postradiation phase are moderately effective (*21–23*) in reducing the mortality and morbidity and in prolonging the survival time.

As stated previously, rats have a high content of properdin in their serums and are also very resistant to bacterial infections. The susceptibility of irradiated rats to severe bacteremia of enteric origin suggested that the properdin system might be destroyed by total body irradiation. Experiments were conducted in collaboration with A. R. Moritz to test this possibility. Large groups of animals were subjected to total body irradiation of 500 r. Blood was collected 2, 7, and 13 days after irradiation, and the serums of each group were pooled. The properdin and complement titers of these serums were compared with pooled serum from untreated animals. Table 6 shows that properdin falls markedly during the early postradiation period. It is noteworthy that complement and complement-component titers increased after irradiation. The low properdin levels reached between 2 to 7 days suggest a causal relationship between the destruction of properdin and the onset of severe bacteremia with subsequent death. While the serums from untreated animals had bactericidal and virus-neutralizing properties, the serums from irradiated rats had lowered bactericidal activity and had little or no virus-neutralizing power.

Stroud and Brues (*24*) have recently reported the partial protection of irradiated mice by the injection of fractions of serum, especially Fraction III (Cohn). Since practically all the properdin of serum is recovered in Fraction III, properdin may be the agent responsible for protection. Indeed, in a preliminary experiment, rats subjected to total body irradiation of 660 r (LD_{90} in 30 days) and injected intravenously with 250 units of purified cow properdin 2, 4, and 7 days after irradiation were partially protected. A control group of irradiated rats injected with saline buffer were not protected.

Further studies are under way to elucidate the mechanism of the loss of properdin in irradiation injury and the role of properdin in irradiation illness. Large amounts of human and bovine properdin are being prepared and will be tested for their efficacy in protecting animals against bacteremia following irradiation.

Role of the Properdin System in Paroxysmal Nocturnal Hemoglobinuria

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare disease in which the patient's erythrocytes are lysed both *in vivo* and *in vitro* by his own serum or by the serum of compatible donors (*25, 26*). No specific hemolysin or antibody against PNH cells has been detected in serum (*25, 26*). Thus, the disease appears to be caused by a defect in the PNH erythrocytes.

Marked similarities were noted earlier (*11*) between the requirements for the inactivation of C′3 by zymosan and for the hemolysis of PNH erythrocytes. Both reactions require Mg^{++} and serum components resembling C′, and both proceed optimally at pH 7. Neither system requires a specific antibody. Stroma prepared from PNH red cells inactivate C′3 at 37°C in a manner analogous to that of zymosan.

Experiments conducted recently with C. F. Hinz, Jr., and W. S. Jordan, Jr., reveal that the inactivation or removal of any factor of the properdin system results in an inhibition of lysis of PNH cells. Serum lacking or deficient in properdin is not lytic for PNH cells, although it contains adequate amounts of all the components of C′ and all measurable elements of the clotting and plasmin systems. The addition of purified human, cow, or hog properdin to serums lacking or deficient in properdin restores the lytic activity of the serum. Properdin alone in high concentrations does not lyse PNH cells. It is also relevant that guinea pig serum, naturally rich in C′, poor in properdin, and inactive in the PNH system, hemolyzes PNH cells after the addition of human or cow properdin or of small amounts of rat serum, which is extremely rich in properdin. These results suggest that the properdin system may be involved in hemolytic phenomena in which a specific hemolysin cannot be demonstrated. E. R. Arquilla (personal communication) has found that the factors in guinea pig serum that are responsible for the lysis of unsensitized sheep cells resemble those of the properdin system. The addition of human or cow properdin to guinea pig serum that has been depleted of properdin restores its full lytic activity.

Appendix 1

Preparation of Reagents for the Titration of Properdin

Serum free of C′3 and properdin (R3). Methods for the preparation of R3 have been described previously (*10, 11*). Special precautions are taken to discard any R3 which, when tested at the two-unit level, is either hemolytic alone or anticomplementary, as judged by failure to give complete hemolysis with one-

fourth of a 100-percent hemolytic unit of C′. An R3 should be capable of measuring 120 C′3 units/ml of RP.

Serum lacking or deficient in properdin (RP). The same amount of zymosan that is required to prepare an R3 is employed to prepare RP. RP is prepared only from serum from which suitable R3 could also be prepared.

Between 2 and 4 mg of zymosan per milliliter of serum is suspended evenly in serum at 15°C to 18°C for 75 min. The control of temperature is important. Temperatures below 15°C result in an incomplete removal of properdin, while temperatures above 18°C result in a loss of C′3 activity in RP. After incubation, the mixture is centrifuged at 4000 rev/min for 15 min at 0°C. The supernantant (RP) is decanted and tested for properdin and for C′ and C′-component activities. If satisfactory, the RP is dispensed in test tubes and maintained at −20°C until needed. In this state, it remains stable for at least 6 wk.

We have established the following criterions for RP. (i) It must have a C′ titer and C′-component titers of not less than 75 percent of the parent serum. (ii) Upon treatment with zymosan at 37°C for 1 hr, its C′3 titer should not decrease more than 25 percent. (iii) It should not be anticomplementary when combined with R3. (iv) It should contain not less than 90 or more than 180 C′3 units/ml when tested against 2 units of R3.

A single treatment of serum with zymosan at 15°C to 18°C is often insufficient to remove all the properdin. Such an RP may be used for the assay of properdin, but it is not always suitable for bactericidal and virus-neutralizing studies. A second treatment of RP with zymosan at 37°C for 15 to 30 min removes all the remaining properdin with only a slight loss of C′ or C′-component activities. This treatment is generally employed for bactericidal and virus-neutralizing studies.

Titration of Properdin

One-half millimeter of RP is added to each of a series of test tubes containing 3 mg of zymosan. Varying amounts of the material to be tested are then added. If necessary, sufficient $MgCl_2$ is added to yield a final Mg^{++} concentration of $5\times10^{-5}M$. Each is made up to a final volume of 1.5 ml with *p*H 7.4 barbital buffer containing $5\times10^{-5}M$ Mg^{++} and is incubated with occasional mixing at 37°C for 1 hr. The mixtures are then centrifuged, and the supernatants are tested for C′3 activity. A unit of properdin is defined here as the smallest amount of serum, body fluid, serum fraction, and so forth, that will result in the loss of 120 units (50 percent end-point), of C′3 from 1 ml of RP in this test system.

A typical protocol for a properdin titration is given in Table 7. The C′3 titers are calculated on the basis that the mixtures of RP, test serum, buffer, and zymosan are at a dilution of 1:3. Sample 9 is a routine C′3 titer on the test serum. Sample 8 is an anticomplementary control. The presence of the test serum should not depress the C′3 titer of the RP; in most instances, it should enhance it. Sample 10 verifies the test and shows that the RP contains all the accessory factors necessary for the inactivation of C′3.

Table 7. A typical protocol for a properdin titration on a normal human serum. The properdin titer is 4 to 8 units/ml of test serum.

Tube No.	RP (ml)	Test serum (ml)	Buffer (ml)	Zymosan (mg)	C′3 titer (units/ml)	
1	0.5	0.50	0.50	3	0	
2	.5	.25	.75	3	0	
3	.5	.12	.88	3	0	} end-point
4	.5	.06	.94	3	tr	} end-point
5	.5	.03	.97	3	30	
6	.5		1.0	3	120	
7	.5		1.0		120	
8	.5	.50	0.5		180	
9		.50	1.0		240	
10	.5	1 standard unit properdin in 0.1 ml buffer	0.9	3	0	

With the present method it is difficult to determine properdin concentrations lower than 1 unit/ml of sample. An assay is being developed to determine the presence of minute amounts of properdin that will involve both this method and a bactericidal test. Methods for the titration of complement and its components have been described elsewhere (*10, 12*).

Appendix 2

Purification of Properdin

Properdin has been isolated in good yield from human and bovine serums by a process that makes use of the specific combination of properdin with zymosan and subsequent dissociation of the properdin-zymosan complex (Fig. 2). The properdin-zymosan complex is prepared by suspending zymosan in serum for 75 min at 17°C, centrifuging the complex, and washing it three times with physiological saline at 1°C. The residue is then dissociated by stirring with a slightly alkaline buffer of ionic strength 0.6 at 37°C; the zymosan is centrifuged down, leaving properdin in the supernatant. The properdin is precipitated from the supernatant by dialysis against distilled water at *p*H 5.8. The precipitate is dissolved in buffer at *p*H 7.5, ionic strength 0.15 and freed of suspended impurities by centrifugation at 25,000 *g*. The supernatant is then centrifuged at 75,000 *g* to yield properdin as a pellet. This process affords a 3000-fold purification of properdin compared with the original protein content of serum on a protein nitrogen basis. An over-all yield of 35 to 50 percent has been consistently obtained.

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Edward Monroe Freeman, Pioneer Plant Pathologist

EDWARD MONROE FREEMAN, pioneer plant pathologist and Dean Emeritus of the College of Agriculture, Forestry and Home Economics of the University of Minnesota, died at his home near the St. Paul Campus of the University on 5 February 1954. Dr. Freeman was born in St. Paul 12 February 1875, attended public schools in his native city, and obtained the B.S., M.S., and Ph.D. degrees from the University of Minnesota in 1898, 1899, and 1905, respectively. Except for 1 year at Cambridge University, England, in 1901–02, and 2 years in the United States Department of Agriculture, 1905–07, Dr. Freeman's professional life was spent at the University of Minnesota, from which he retired to emeritus status in 1943.

Not only was Dr. Freeman one of the most eminent of the pioneers in the development of scientific plant pathology in the United States, but he also contributed significantly to the development of a broader and deeper scientific basis for education and research in the general field of agriculture. He was especially well qualified for his extraordinary contributions by exceptional native ability, a liberal education, and wide experience.

Freeman's education was unusually extensive and intensive. He did not have formal education in agriculture; he studied in the College of Science, Literature and the Arts of the University. And he actually studied sciences, literature, and the arts. Everything interested him but especially the sciences. For a time he studied mathematics, astronomy, physics, chemistry, geology, zoology, and botany with approximately equal avidity. Gradually, however, he developed special interest in zoology and botany and finally chose botany as his major in graduate work.

It was characteristic of Freeman that he tried to learn everything possible about everything that he decided to study. It is natural, then, that he acquired unusually extensive knowledge about the plant kingdom—slime molds, algae, fungi, liverworts, mosses, ferns, and seed plants. He became an exceptionally good general botanist. But the fungi finally captured his special interest, partly because they were so interesting in themselves and partly because they were so important as parasites on other plants. Freeman never lost interest in the evolution and nature of parasitism, but he also developed a very deep interest in preventing the devastating effects of fungus parasites of economic plants. He became a plant pathologist.

As a plant pathologist, Freeman developed concepts and charted fields of investigation that contributed richly to the understanding and control of plant diseases. His concepts were compounded of shrewd speculation, tempered by thorough scientific scholarship, and buttressed by results of keen observation and persistent experimentation. He was essentially curious, imaginative, and speculative, but he was practical also. He had a passionate interest in the facts and theories of science, but he also had an impelling desire to learn their practical values. As a graduate assistant, he taught pharmacognosy; he went to Cambridge to study plant parasite-host relationships in the laboratory of the eminent Marshall Ward; as assistant professor of botany in an academic department, he gave courses in economic botany and plant pathology and in 1905 he published the 400-page book, *Minnesota Plant Disease*.

In the preface to his book, Freeman emphasizes the

need for basic understanding of plant diseases and for wider dissemination of knowledge regarding their causes and control. In his own words,

> Upon such knowledge, widely disseminated, can be built a substantial system of disease prevention. In short, the aim of this work is rather educational than immediately practical, for in the former feature the author hopes that it will be ultimately most useful.

In autographing a copy of the book in 1948, Dr. Freeman wrote,

> I realized that this book could not then be more than a crude, inadequate and pioneering presentation of and in its field. But it was to me, in a very real sense, the expression of a dream of a life-long scientific adventure and profession in the new, attractive and useful field of plant pathology. Now, almost 50 years later, I find that dream more completely realized than I ever had reason to hope for. . . . But I am not deluding myself. I furnished a dream; the symbol is *Minnesota Plant Diseases*. . . .

A dream, a symbol: the dream and symbol of a scientific pioneer who loved the academic tradition but loved also to help solve human problems by the application and dissemination of science. Freeman loved people as well as science; he loved research and he loved teaching.

> It is a very evident fact that all agricultural pursuits are taking great strides, and the education of those boys and girls who are about to cultivate or manage the cultivation of lands is becoming more and more imperative.

This quotation from the preface to *Minnesota Plant Diseases* presages the final phase in the application of Dean Freeman's talents.

On 1 August, 1907, Dr. Freeman was appointed chief of the newly created Division of Vegetable Pathology and Botany in the College of Agriculture of the University of Minnesota, the first department of plant pathology in an American university. Returning after 2 years' service in the United States Department of Agriculture, he immediately began to organize teaching and research in plant pathology and agricultural botany. And, characteristically, he combined the basic with the applied. He laid the foundation for a sound program of instruction, research, experimentation, and public service in his own department and helped significantly in raising standards in the entire institution. He enthusiastically promoted activities ranging from the establishment of a seed-testing service for farmers to studies on the phylogeny of fungi; and he was one of the early pioneers in breeding for disease resistance in crop plants.

But Dr. Freeman's genius for dealing with students was soon recognized, and more and more he was pressed into official positions in the College of Agriculture. After serving for several years as chairman of the Students' Work Committee, he was appointed assistant dean of the College in 1913, and dean of the College of Agriculture, Forestry and Home Economics in 1917. The College was one of the units of the Department of Agriculture, now the Institute of Agriculture, of the University, which included all agricultural activities, under the administrative supervision of a dean and director. Freeman therefore was essentially dean of undergraduate students, but he also contributed greatly, officially and unofficially, to the development of high standards in graduate work in agriculture. He also continued as chief of the Department of Plant Pathology and Botany until 1940, for, despite his devotion to students, he remained devoted to his science.

Few men have sacrificed so much as Dean Freeman of personal desire and ambition to the welfare of students. He had insatiable curiosity and an emotional zeal for understanding scientific phenomena. But he had equal zeal for understanding students and their problems; and, inevitably, the problems of students took precedence over his own. He never complained but merely regretted that time and energy did not suffice for both. When a choice had to be made, however, he chose the students and denied himself.

Dean Freeman incarnated the principle that everyone was entitled to education in proportion to ability and desire, and he succeeded in organizing curriculums accordingly. Every student was an individual phenomenon to him, worth as patient and thorough study as any scientific phenomenon; but every student was also a human being, worth understanding, encouraging, and helping toward a life of happiness and usefulness. And, if it seemed that discipline would be helpful, there was no hesitation in applying it. But discipline was always tempered with mercy born of understanding and sympathy. The barriers between student and dean, between youth and age, melted away under the dean's warm and sympathetic personality. Almost universally students looked serene when emerging from his office, even after reprimand or sentence of punishment, for they realized that their troubles were the dean's troubles, that justice had been done, and that they themselves had helped formulate the verdict.

Dean Freeman's personality and contributions are a vivid memory to those who knew him. Although future generations of students and investigators cannot know him as he really was, they will still owe him a deep debt. His dreams were translated into sound concepts by his scholarship; his concepts were translated into effective and far-reaching programs by his skill and wisdom. Time may dim the memory of the man but many future generations will continue to profit by his works.

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Suggested Extension of the Grenville Orogenic Belt and the Grenville Front

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In recent years much evidence has tended to show that the area of the Canadian Shield designated as the Grenville subprovince by M. E. Wilson (*1*) and as the Grenville province by J. E. Gill (*2*) was mountain-built in later pre-Cambrian time. Both Gill and J. Tuzo Wilson (*3*) have discussed its relationship to other major features of the Shield. Determinations of ages of radioactive minerals in the Grenville province fall within the range 1100 to 800 million years (*4–7*). However, there are many unanswered questions concerning the relations of the uraniferous pegmatites to the orogeny or orogenies that have affected the region.

The province is approximately bounded on the southeast by the St. Lawrence River, but with the Adirondack Mountains as a southeastern outlier (Fig. 1). The northwestern border of the province lies about 250 mi northwest of the St. Lawrence. This boundary is known as the Grenville front (*8*).

The extent of the Grenville orogenic belt is not yet fully established. J. Tuzo Wilson (*9*) suggested that it is truncated at the northeast (outside the limits of Fig. 1) by the Labrador orogenic belt, but later he seems to have regarded the relationship an open question (*3*). The linears shown on his earlier map may allow the interpretation of the two belts as contemporaneous. Their junction is rather similar to that of the eastern Himalayas with the north-south Burma ranges. Alternatively, the Labrador belt may be older than, and truncated by, the Grenville. This latter interpretation is supported by a few age measurements of about 1500 million years in the Labrador belt and has been adopted by Collins, Farquhar, and Russell (*10*) in a recent revision of Wilson's map that shows the Grenville fault zone passing into the Atlantic on the Labrador coast north of Hamilton Inlet.

To the southwest, the Grenville belt passes out of sight under early Paleozoic sediments north of Lake Ontario, with no indication of diminished intensity of folding, if we may judge from the intricate structure in the Hastings district (*11*). It could be expected to continue for some hundreds of miles. Directly along its strike lie three anticlinal structures in the Paleozoic rocks. In order, from northeast to southwest, these are (i) the Findlay arch, (ii) the Cincinnati dome, and (iii) the Nashville dome (Fig. 1). It is suggested that these broad, gentle upwarps are the present surface expression of the Grenville mountain range.

After the Grenville orogeny and the intrusion of the Killarney granite, the mountains were eroded and perhaps peneplaned. According to current tectonic concepts, such an orogenic belt typically develops a deep "root" of sialic material and is persistently buoyed up by the underlying sima, while being reduced by erosion. The Cincinnati and Nashville domes throughout Paleozoic time were alternately shallowly submerged and slightly exposed above the sea, while adjacent areas to east and west sank more consistently and received thicker deposits of sediments (*12*). The Grenville orogeny may be the reason for the existence of these anticlines, which continued to rise isostatically or, at least, to sink much less rapidly than neighboring areas. That the belt now appears as a group of domes may be conjecturally attributed to variable depth or intensity of deformation at different places.

Probably the most striking feature of the structure in the southern United States is the great offset of the Ouachita Mountains folded belt relative to the Appalachians. Details of the displacement are concealed beneath Cretaceous and Tertiary sediments of the Mississippi embayment. It is noteworthy that the relationship of the Ozark uplift to the Ouachitas is practically identical with that of the Nashville dome to the Appalachians (*13*). It is as if the Grenville belt were offset in the same direction and about the same amount as the belt affected by the late Paleozoic orogeny.

It is therefore suggested that the Grenville mountain range originally curved smoothly from a southwesterly to a westerly trend near the present Mississippi River and that a great fault of later (but still pre-Cambrian) date cut across it at the bend and dislocated the western side (the Ozark uplift) horizontally northward 200 mi or more. It is further suggested that this fault and the known Grenville front in Canada *may be one and the same*. The resulting trace is fairly straight. The Grenville front disappears under Lake Huron at Killarney, Ontario. The proposed extension would pass, beneath Paleozoic rocks, through the "thumb" of Michigan, the extreme northwestern corner of Ohio, southwestern Indiana, and approximately along the Mississippi River between Arkansas and Tennessee (Fig. 1).

If such a displacement of the Grenville belt did occur, there seems to be no possibility that it took place later than the end of pre-Cambrian time, for none of the Paleozoic rocks along its suggested course show large disturbance. If this hypothesis is correct, the equal dislocation of the Appalachian-Ouachita belt must be due to the circumstance that the uplift

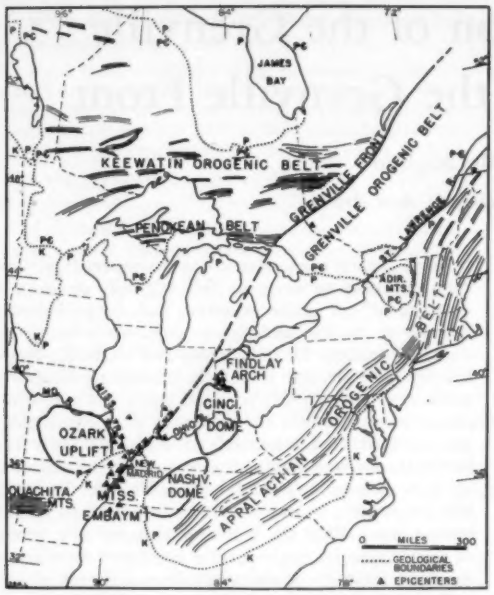

Fig. 1. Sketch map showing relationships of major structural features of eastern United States and Canada, including the Grenville front and proposed extension (heavy dashed line). Earthquake epicenters distant from the extension are not shown. *PC*, pre-Cambrian; *P*, Paleozoic; *K*, Cretaceous and Tertiary.

of the old Grenville belt determined the northwestern and northern limits of the Paleozoic geosyncline.

That the exposed part of the Grenville front in the Canadian Shield is a great fault zone now appears very probable. Areas along the boundary have been studied in detail by Quirke and Collins (*14*), Cooke (*15*), Fairbairn (*16*), Norman (*17, 18*), and Tiphane and Dawson (*19*). In particular, Norman, Tiphane, and Dawson (*20*) have called attention to the Grenville front as "a fault zone of continental proportions." In all the reports just mentioned, the rocks near the contact are described as intensely crushed and sheared (in some places for a width of more than a mile). All agree that the gneisses of the Grenville province have been thrust northwestward on the Huronian, Keewatin, Timiskaming, and intrusive rocks of the adjoining Superior province to the west.

Along the greater part of the Grenville front, it has been found impossible to identify formations across that boundary. The east-trending folded belts of Keewatin and Timiskaming volcanics and sediments of northern Ontario and Quebec represent the oldest known orogenic belt in the Canadian Shield, for which radioactive determinations yield ages around 2200 to 2500 million years (*6, 21*). These folded rocks are cut off abruptly at the Grenville front, and no recognizable equivalents have been identified farther east along the continuation of their strike. Farther south, near the north shore of Lake Huron and through northern Michigan and Wisconsin, the Penokean folds involve the Bruce and Cobalt series and the iron formations and associated sediments, all of Huronian age. Although recent work in Ontario (*22*) has reopened the question of equivalence of the Bruce series and the Timiskaming, the radioactive age measurements give figures clustering about 1300 million years for this belt (*6*), making the Penokean orogeny distinctly younger than that which affected the Keewatin-Timiskaming belts farther north. The Penokean folds are likewise truncated by the Grenville front. However, Quirke and Collins (*14*) identified some large remnants or "inclusions" of metamorphosed Huronian rocks in the Grenville gneisses near Killarney, and Quirke (*23*) found some as far as 20 mi east of the Grenville front. Nevertheless, the transition from Huronian sediments to gneisses at the front was abrupt.

The faulting along the Grenville front was post-Mistassini (*18*), post-Cobalt, and post-Penokean, but it was pre-Killarneyan, for Cooke (*24*) found Killarney granite invading and obliterating the fault zone southeast of Sudbury. Quirke (*25*) found similar relationships near Killarney. The most significant observations, for our present purpose, are those of Cooke. He found evidence of two faulting movements. The first apparently determined the major displacement, and all the evidence indicated that *the southeastern block moved not only upward, but southwestward as well, relatively to the northwestern block.* This is consistent with my suggestion that the Ozark uplift was displaced northward along a continuation of the Grenville fault zone. The later movement apparently coincided with the intrusion of the Killarney granite; it was also upward on the south, but in the opposite horizontal direction. Unless I have misinterpreted Cooke's statements, this later movement was not evident except in those localities where granite was intruded along the fault. The displacement was probably of much smaller magnitude than the earlier movement. This evidence appears favorable to the suggested large motion along the fault in a direction required to make the Ozark uplift a former extension of the Grenville orogenic belt.

The apparent impossibility of recognizing formations across the Grenville fault zone may then be due, not only to metamorphism, but to the existence of an offset of 200 mi or more. This is comparable with the recently suggested cumulative displacement along the San Andreas fault (*26*).

The intrusion of the Killarney granite may be supposed to have welded the old fault at many places. Certainly no extensive movement occurred during the Paleozoic and later periods. However, it seems possible that the old fault is not entirely dead, more especially near the southern end of its hypothetical continuation. A large number of earthquake shocks have been felt near the confluence of the Ohio and Mississippi rivers. The New Madrid earthquake of 1811 was one of the most violent known. A recent map (*27*) shows a strong concentration of epicenters (Fig. 1)

trending northeastward from the vicinity of New Madrid into southwestern Indiana, where it suddenly terminates. These do not seem to be related to the Rough Creek fault zone (*28*), for they trend across it, rather than along it. Their trend is parallel to the hypothetical trace of the Grenville fault zone and to a number of small faults in the Paleozoic rocks, which may be the surface expression of vertical movements on the buried Grenville fault. Another compact group of epicenters in western Ohio is some 50 mi east of the suggested trace of the fault. These would not be inconsistent with an eastward-dipping fault zone. Finally, a strong shock originated near Timiskaming, Quebec, 1 November, 1935. This locality is about 25 mi east of the Grenville front. The epicenter seems to have been well determined, but the depth of focus, tentatively indicated as 200 km (*29*), later proved to be indeterminate (*30*). It is probably an open question whether this earthquake was associated with the Grenville front or with the Timiskaming lineament (*31*).

Since the preceding paragraphs were written, my attention has been called to a group of reports (*32–34*) on areas near the supposed course of the Grenville front in Quebec, about latitude 49°30′, longitude 74°30′. In three adjacent 15-min quadrangles, the Keewatin-type lavas and associated meta-sediments were found increasingly metamorphosed toward the east and also showed increased complexity of folding in the same direction. Judging from the prevalence of hornblende and biotite paragneisses, the Grenville belt seemed to have been entered, but no major fault was located, although the eastern area lies athwart the front, as is shown on the Tectonic Map of Canada. Either the front passes farther east, or it is locally obscured by intrusives, or it is discontinuous. This last alternative, if conclusively demonstrated, would of course be a most serious difficulty for the hypothesis here proposed. Evidently much additional work will be required before the major structure can be considered fully established.

I am indebted to E. N. Goddard and James T. Wilson of the Department of Geology, University of Michigan, for a critical reading of a first draft of this article, but this does not imply agreement with the views here expressed.

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With the consent of the author, we quote these remarks made by two of our advisors: "This paper involves a high degree of speculation, but is sufficiently intriguing and stimulating as an example of what W. M. Davis called 'outrageous hypotheses' [Science **63**, 463 (1926)*] to be a 'must' for publication." "It is thought provoking, stimulating, and challenging—inviting confirmatory observations on the one hand and exposing the author to sharpshooting critics on the other."*

News and Notes

Genetic Recombination

The Seventh Annual Symposium of the Biology Division of the Oak Ridge National Laboratory, held 19–21 Apr., with the Atomic Energy Commission as cosponsor, was devoted to the subject of genetic recombination. This was a most timely subject, because the recent work on genetic recombination in viruses and bacteria and the recent developments in the knowledge of the chemical composition and structure of the genetic material clearly need to be integrated with the older knowledge of crossing over obtained from the genetic analysis of recombination in *Drosophila*, maize, *Neurospora*, and other organisms. Six sessions were devoted to a thorough reconsideration of the perplexing nature of genetic recombination, in the light of the latest findings in such relevant areas as bacterial transformation and transduction, genetic recombination in bacteriophage and bacteria, chromosome replication and behavior, the structure of the desoxyribose nucleic acid molecule, and recombination in natural populations.

The first session was opened with a masterly review by Rollin Hotchkiss of recent work on the *Pneumococcus* transformations, a review that served as a setting for all the discussions that followed. The most interesting recent observation in this field is probably that of the separability of genetically determined characteristics in the transfer process. Thus, if an encapsulated, drug-resistant strain is used as a source of desoxyribose nucleic acid (DNA) for the transformation process, separate encapsulated and drug-resistant types are induced in the recipient strain. A penicillin-resistant strain that had acquired its resistance by steps yielded DNA that also induced resistance in the recipient in a stepwise transformation, the individual steps being in the same sequence in the original acquisition of resistance and in the transformation process.

Experiments with the adaptive enzyme mannitol dehydrogenase showed that DNA from the *M*-strain transformed cells of the *m*-strain irrespective of whether the enzyme was actually present in the cells of the *M*-strain. In other words, it is not the enzyme itself, but the genetic material that is transferred from strain to strain. DNA from a strain with the mannitol-fermenting enzyme and also with streptomycin resistance produces transformed strains with the former character or the latter singly, or with both together; and the reciprocal type of recombination, which yields the double type from a recombination between two donors of the single types, is also obtainable. Desoxyribonuclease completely blocks the transforming process; and DNA from calf thymus also inhibits the transformation by means of pneumococcus DNA. From these and other results, including the inability to detect any other substance in the purified DNA used for the transformations, Hotchkiss concluded that the genetic material is DNA itself, rather than protein or nucleoprotein. The recombination of different genetic characters in the DNA-transformations implies that the DNA is diversified—that is, it exists in the form of different "genes." Vigorous discussion and debate were aroused by the presentation of these concepts.

Norton Zinder followed with a similar story, that of bacterial transduction in *Salmonella*. In this phenomenon, phage is the transducing agent in the transfer of a genetic trait from one strain of the bacterium to a different strain. Linked transductions have been discovered. Since the active part of the bacteriophage is DNA, the interpretation of this phenomenon reinforces the conclusions reached by Hotchkiss. A. H. Doermann described the genetic recombination process in the bacteriophage itself. In the T2 and T4 coliphages, three distinct linkage groups have been identified. When the phage particle infects the host cell, its protein membrane is left outside and only the DNA (genetic material) enters the host cell. Here, after multiple infections, recombination may occur even between genetic units supplied by three different phage types. There is not as much interference to recombination in both of two linked regions as there is in the higher organisms; in fact, there is more recombination than is to be expected on the simple basis of an independent coincidence of recombination in the two regions. X-rays can inactivate some genes in a phage particle without damaging others. This fact, like the recombination process, indicates the independence and integrity of individual genetic units.

Joshua Lederberg, following the preceding speakers, discussed recombination in bacteria. The recent development in this field that has clarified considerable doubt and confusion, resulting from the inability to find sexual recombination in any bacteria other than *Escherichia coli* K-12, has been the discovery of the dependence of mating and recombination on differences in mating type. The situation somewhat resembles that which is now so well known in *Paramecium* and other protozoans. Thus, crosses between F− and F− are sterile, and crosses between F− and F+ are uniformly fertile, yielding only F+ progeny; but, on the other hand, crosses between F+ and F+ are also somewhat fertile. Another significant finding is the discovery that certain strains will cross when they are treated with streptomycin, whereas they will not cross if untreated.

On the second day, discussion began with a very interesting paper by J. D. Watson on the relationship between the structure of the DNA molecule, as worked out by Crick and Watson, and the processes of chromosome replication and recombination. DNA fibers 20 A in diameter and many thousands of angstrom units in length give x-ray diffraction patterns that imply the presence of double, rather than single, chains. Crick and Watson have postulated a model consisting of two intertwined chains with 10 nucleotides per coil, and with the phosphate-sugar groups

outside and the base groups inside. The latter are united between strands by H bonds that link adenine to thymine and guanine to cytosine, this structure being the only one that allows the coiled chains to fit properly and that is consonant with the observed ratios of 1 purine : 1 pyrimidine, 1 adenine : 1 thymine, and 1 guanine : 1 cytosine. Replication might occur if each fiber separated from the other and then served as a template. Secondary phosphoryl liberations indicate that there are breaks in the chains at intervals of 50 A. Genetic continuity might be assured if the breaks in the sister strands alternate in position; and crossing over may be related to replication.

David D. Perkins discussed methods for extending the analysis of crossing over, particularly in such forms as *Neurospora*, by relating chiasma interference, chromatid interference, and possibly sister-strand crossing over to the observed frequencies of various types of tetrads and multiple exchanges and to recombination frequencies. Edward Novitski and Drew Schwartz presented some recent work on chromosome behavior and crossing over in *D. melanogaster*. Novitski described the six possible types of compound X-chromosomes, which synapse either spirally or by a simple foldback of the two components. Crossing over between the two components of these compound X's throws some new light on the crossing-over process. Thus, in a tandem compound-X carrying an inversion in one component X, crossing over is reduced within the inversion to about one-fourth of what would be expected in the absence of an inversion. Yet there was no striking interference between a crossover outside the inversion and one inside it. The conclusion may be drawn that pairing between the chromosomes is initiated by the heterochromatin, and that a weaker euchromatic pairing commences when homologous euchromatic regions are brought into proximity. Schwartz, from analyses of crossing over in maize as well as in *Drosophila*, has come to the conclusion that sister-strand crossing over, long thought to be ruled out by classic observations, must be postulated in order to explain his data on anaphase configurations resulting from crossing over in ring-rod heterozygotes in maize, and on twin spots produced by somatic crossing over in *Drosophila*.

In the final session, Maurice B. Whittinghill summarized the effects of ionizing and ultraviolet radiations on crossing over, and dwelt particularly on the induced crossing over in gonial—oögonial as well as spermatogonial—cells. Hampton L. Carson discussed the relationship of genetic recombination to the amount of genetic variation in natural populations, particularly those of *D. robusta*. Populations at the center of the distribution of a species seem to show more blocked recombination because of the presence of heterozygous chromosome rearrangements. Populations toward the borders of the distribution of a species are more homozygous as to chromosome arrangement; hence, they have freer recombination and, consequently, manifest more genetic variation.

Alexander Weinstein, A. H. Sturtevant, and Karl Sax undertook to summarize and evaluate the various contributions made to the symposium, including the points of view developed in the vigorous and often entertaining free discussions that followed the formal papers. These evaluations by veteran students of the recombination process were particularly welcome.

On the first evening of the meeting, an extra session was scheduled for those persons particularly interested in a field in which the Oak Ridge workers themselves have been leaders, namely, the study of the effect of oxygen concentration on the induction of chromosome aberrations by x-rays. Work with *Tradescantia* and *Drosophila* was presented by Norman H. Giles, Jr., C. P. Swanson (paper read *in absentia*), and W. K. Baker. Others who were present added data that throw light on the relative merits of the hypotheses that oxygen exerts its effect by either affecting recombination or affecting the initial frequency of breakage.

An opportunity was given the approximately 150 participants in the symposium to visit the Biology Division of the Oak Ridge National Laboratory. There was opportunity for informal discussion between visitors and hosts alike on problems of mutual interest. The symposium was declared to be one of the most successful ever held at Oak Ridge. Like the previous Oak Ridge symposia, it is planned to have the proceedings published as a supplement to the *Journal of Cellular and Comparative Physiology*.

BENTLEY GLASS

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AAAS Southwestern Meeting

The 30th annual meeting of the Southwestern Division of the AAAS was held 25–29 Apr. in Lubbock, Tex., at the Texas Technological College. This was the third time that the Association has enjoyed the hospitality of Lubbock and the College, the earlier occasions having been in 1934 and 1941, and the growth of both the city and the school during this 20-yr period is phenomenal. Joining in making the meeting a success was the Southwestern Association of Naturalists (SWAN). Although organized only a little more than a year ago, it has already become an important factor in fostering scientific progress in the region. Other cooperating societies were the Texas and Oklahoma academies of science, the Texas Archaeological Society, and the Panhandle Plains Section of the American Chemical Society. Under the auspices of the society of the Sigma Xi, Henry Eyring, dean of the graduate school of the University of Utah, delivered an after-dinner speech on "The physical chemistry of enzymes in luminescent bacteria and nerves."

Ever since the Southwestern Division was organized in 1920, a great deal of its interest has centered around problems peculiar to arid lands. In the early days, this interest took the form of archeological studies of the prehistoric peoples who once lived in the area, and several years ago the Division set up a special committee on desert and arid zone research. Through its

efforts, the UNESCO committee on arid lands has become so interested in the Division's work that it has agreed to give some support in organizing an international symposium to be held in Albuquerque, N.M., following the Southwestern Division's meeting in Santa Fe in Apr. 1955. After the symposium there will be a conference at Socorro with the New Mexico Institute of Mining and Technology as host. Plans for these arid lands meetings have been discussed at length [*Science* **119**, 869 (18 June 1954)].

The annual John Wesley Powell lecture was given this year by Roger J. Williams, biochemist of the University of Texas. The title he chose for his address was "A new era in human understanding." Four symposia dealt with "Instrumentation," "Ground water of the south plains of Texas," "Natural history of the Lubbock area," and "Geology and oil technology." Some idea of the wealth of material presented can be gleaned by noting such titles as "Radiological instrumentation," "Application of transducers in the measurement of physical quantities," "Underground water flow," "The use of fish embryos in biological assay tests," "Differentiation in call among southwestern anuran amphibians," "The interpretation of seismic data obtained in geophysical prospecting," "The internal plastic coating of pipelines in place," "The use of emulsions to stimulate petroleum production," and "Radiotracer survey as a gas and oil well service."

Eight papers in the social-sciences section included such titles as "Some repeated pictograph forms in the Big Bend of Texas," "Acculturation of the Navajo Indians," and "Human sterilization laws and psychiatric thinking." Some of the 23 botany papers treated "Successional relations of plant communities of the Elk Mountain Range," "The effect of certain soil correctives on nutrition of seedlings," "Evolution of college botany teaching," "Ladies botany," "The absorption of 2,4-D through the root systems of 60 woody plants," and "A study of some factors affecting the quality of cottage cheese." Some of the topics for the 11 papers in the field of zoology were "Birds of the south plains," "The nasal mites of finches," "The effect of certain chemicals on the eggs and larvae of the dog hookworm," and "Inhibition of antidiuretic activity of blood serum with adrenal medullary hormones."

There were 31 papers in the physical sciences and among them were "Parallax in mathematics," "Influence of planetary alignment cycles on climatic variation," "Ion exchange in clays," "A spectrographic study of the venoms of some poisonous desert animals," "The effects of ionizing radiations on the chemical composition and carcinogenicity of organic and biochemical compounds," "A polarographic study of the zirconium-alizarin lake," "The motion of a conducting sphere in a uniform magnetic field," "Elastic scattering of fast neutrons," and "The fluorescence of alpha naphthylphenyl oxazole in various solvents."

About 300 persons registered at the meeting, many of them coming from states well beyond the limits of the Division. At the closing business session, it was voted to recommend to the national office that the Division's name be changed to Southwestern and Rocky Mountain Division, in view of the fact that Wyoming and a part of Montana had recently joined. Joe Dennis of the Texas Technological College and E. F. Castetter of the University of New Mexico were elected president and vice president, respectively. Frank E. E. Germann of the University of Colorado was continued as secretary-treasurer.

FRANK E. E. GERMANN
University of Colorado, Boulder

Science News

The Soviet Council of Ministers has announced that a 5000-kw electric **power station using atomic energy** is in operation somewhere in Russia. The station, which may be regarded as only a pilot model, was described in the announcement as "the first industrial electric station utilizing atomic energy."

An extensive **analysis of the American Medical Association** by the student editors of the *Yale Law Journal* criticizes the A.M.A.'s excessive authority over medical practice and its failure to use this power as an "instrument of progress." The 84-page report, published in the current issue of the *Journal* contains both criticism and praise for the A.M.A., but the criticisms predominate; it is based on a 2-yr study of the A.M.A.'s published records, interviews with both its critics and proponents, and a questionnaire directed to state medical societies.

In Chicago, George F. Lull, secretary and general manager of the American Medical Association, who received an advance copy of the report shortly before it went to press, issued a strong statement in rebuttal. "It took the students two years to make the study, but they took neither the time nor the trouble to interview A.M.A. officers or staff people at the Chicago headquarters to get their facts correct. It is most unfortunate that the article was submitted to us so late that insufficient time remained before publication for correction of basic and glaring errors of fact and omissions of vital facts. In many important sections the text is based on completely false and erroneous information."

The report states that "no other voluntary association commands such power within its area of interests as does the A.M.A. It holds a position of authority over the individual doctor, wields a determining voice in medical education, controls the conditions of practice, and occupies a unique position of influence in shaping government health policies." For example, the authors charge that the A.M.A.'s power has been used to block virtually all plans for providing low-cost health and medical care unless subjected to Medical Association control; at present, the article continues, the A.M.A. is opposing President Eisenhower's proposal for Federal Government reinsurance of voluntary health plans on the thesis that this might lead to socialized medicine. In rebuttal, Dr. Lull said that the "Association opposed the federal

reinsurance plan because it was unnecessary and represents the intrusion of the Federal Government into a phenomenally successful area of private enterprise. Evidently the House of Representatives felt the same way because it recently 'killed' the bill by an overwhelming majority—238 to 134."

The *Yale Law Journal* pointed out that although many physicians are critical of A.M.A. policies, the A.M.A., with its total national income of $9,000,000 a year, is not truly representative of the nation's doctors and does not tolerate conflicting opinions within its membership. The article claims further that the *Journal* of the A.M.A. "rarely prints opinions in disagreement with positions taken by the organization's governing boards." Dr. Lull branded this statement as false. "On the contrary, the A.M.A. is so representative of its membership that many other organizations, including the American Bar Association, have modeled their organizational structure after the A.M.A."

Physicians who defy A.M.A. authority, the law students argue, may be subjected to professional ostracism, which could cut them off from patient referrals and consultations, deny them advancement in hospitals, or bar them from professional appointments. Dr. Lull also branded this statement as false. "The American Medical Association has almost no authority over individual physicians. It is the county medical society that disciplines members who are guilty of unethical practices."

"Despite the dangers inherent in such a concentration of power," the Yale report continues, "no interest group enjoys more freedom from federal control than organized medicine."

Several steps are recommended by the student authors to curb these powers. First, to protect the individual doctor from unreasonable exercise of organized medicine's authority, the importance of society membership should be de-emphasized in order to mitigate the severe consequences of its disciplinary powers. As one step, the writers suggest that this could be done by insuring availability of hospital privileges to nonmembers. Commenting on this statement, Dr. Lull said, "the American Medical Association has no control whatsoever over hospital staff appointments which are made by the local hospital Board of Trustees."

The second recommendation urged that organized medicine should be divested of its control over the nation's supply of doctors. This step could be accomplished by federal aid to medical schools without impairing A.M.A. powers to set educational requirements and to inspect these schools. Dr. Lull termed this accusation "false and malicious." The A.M.A. he said, "has no control over the nation's supply of doctors. The Yale Medical School Admission Committee and all similar committees throughout the United States determine the number to be admitted. The A.M.A. has nothing to do with control over the supply of doctors."

The student authors also recommend that legislatures should divest state medical societies of their control over the formation of new methods of providing low-cost prepaid care. At present state statutes requiring approval or participation by the medical society or a majority of the doctors have foreclosed experimentation in solving pressing medico-economic problems. "Independent groups of doctors, cooperatives, unions and employers—as well as the medical societies—should be free to work out their own solutions. Government assistance to plans for low-income subscribers may also be required."

Finally, the authors say, the A.M.A. should provide a forum for dissenting opinions and conflicting viewpoints. "New ideas which the A.M.A. has accepted have been forced upon it; by assuming leadership in experimentation with unproved systems of practice and payment, the A.M.A. could become an instrument of progress."

Dr. Lull in his concluding statement of rebuttal to the student report said: "The real danger in this article is that nearly all of the facts are given a negative slant whereas they just as well could have been presented in a positive light. It is very apparent that the authors built up a straw man and then proceeded to knock him down. It is an obvious attempt to neutralize the conservative influence of one of America's great voluntary health organizations."

An **artificial heart** of Swedish design was used for the first time to save a human being on 16 July when Clarence Crafoord operated upon a 42-yr-old woman suffering from a growing tumor of the heart. The operation is reported to have been successful. The artificial heart, designed by Åke Senning and Anton Åstradsson, is based on a method of producing controlled "ventricular flutter" by means of weak electric shocks.

The **U.S. Naval Engineering Experiment Station,** Annapolis, Md., marked its 50th anniversary in July. Located across the river from the Naval Academy, it covers 50 acres and maintains a staff of 1000.

Discovery of a **6000-yr-old canal system** that ran parallel to the Euphrates River in ancient Mesopotamia has been announced by Albrecht Goetze, professor of Assyriology and Babylonian Literature at Yale, and director of the Baghdad School of the American Schools of Oriental Research. While archeologists had long known of sections of this canal, they were unaware of the complexity and extent of the system until it was traced by a recent expedition to Iraq sponsored by the American section of the Baghdad School of Oriental Research.

The work was headed by Thorkild Jacobsen of the Oriental Institute of the University of Chicago. Vaughn Crawford, research fellow in the department of near eastern languages and literature at Yale, was a member of the expedition. The system was used mainly for irrigation, although it served also as one of the main lines of communication between towns. The ancient towns of Bad Tibira and Zabalam were located, and findings have led to the correction of earlier archeological views on the location of Lagash, one of

the first Sumerian towns ever excavated. The canals were abandoned probably in the era of Hammurabi about 1800 B.C.

At the Seattle meeting of the American Physical Society in July, Marcel Schein of the University of Chicago reported that a very unusual new event consisting of a **large number of individual electron pairs** has been found in a stack consisting of 18 Ilford G-5 600-μ pellicles flown in a Skyhook balloon from Goodfellow Air Force Base, Tex. (41° N. geomagnetic latitude). The pellicles were placed in an aluminum exposure box with 0.7 gm/cm²-walls and free of other matter. The emulsions were exposed for 6 hr at an altitude exceeding 100,000 ft. The event entered the side of the stack at a zenith angle of 66° and passed through 14 of the 18 pellicles with a total length of more than 50,000 μ and at an angle of 7.5° to the emulsion surface. This made it possible to carry out accurate measurements on individual tracks. An explanation of this event by conventional mechanisms has not been possible. Hence the tentative suggestion was offered that it may be due to annihilation of an antiparticle, a negative proton. Production of antiparticles at these energies by cosmic ray particles outside the atmosphere is predicted by Fermi's theory.

The national birth total in the first four months of 1954 topped the same period of 1953 by about 30,000, according to **vital statistics** estimates released recently by the Public Health Service of the U.S. Department of Health, Education, and Welfare. However, marriages this year have continued to fall, after sinking in 1953 to 9.7 marriages per thousand population, the lowest annual rate since 1933. Compared with the first four months of 1953, marriages in the same period this year dropped by 25,000, a drop of 7.2 percent.

In connection with the **visa problem,** it is interesting to note that the Secretary of State has recommended that 11 churchmen from Czechoslovakia and Hungary be admitted to the United States as official deleates to the second assembly of the World Conneil of Churches at Evanston, Ill. Among the other Protestant church meetings of international significance taking place in the U.S. this summer are the Presbyterian Alliance Conference at Princeton University and the World Lutheran Conference in Chicago.

Hexamethonium chloride, given with alseroxylon, a derivative of *Rauwolfia serpentina,* benefited 36 of 39 hypertensive patients and brought **blood pressure** down to normal levels in 18, according to a report in the 17 July issue of the *Journal of the American Medical Association* by W. R. Livesay, J. H. Moyer, and S. I. Miller, Baylor University College of Medicine.

When the *Rauwolfia* derivative was given alone to 43 additional patients with high blood pressure, 20 responded favorably, and 10 returned to normal blood pressure levels. Alseroxylon given with hydralazine to a third group of 21 patients lowered blood pressure in 12 and brought a return to normal levels in one. Fewer side effects were observed when the drugs were used in combination than with hexamethonium alone.

In cases of mild or fluctuating high blood pressure, the less potent *Rauwolfia* derivatives such as alseroxylon should be given alone as the initial treatment. When severe high blood pressure is complicated by kidney failure, alseroxylon should be used with hydralazine rather than with hexamethonium, because of the lower potency of the former. Severe malignant hypertension or hypertensive emergencies call for hexamethonium given by injection or infusion.

On 28 July L. Kresak and M. Vozarova, both of the Skalnate Pleso Observatory in Czechoslovakia, discovered a **new comet,** their second such discovery in July. Now known only as 1954 F, it is of magnitude 9 and is in the constellation of Camelopardalis. It is the sixth new comet to be spotted this year. With a small telescope and good visibility, it can be seen most of the night.

Herman A. Spoehr, retired chairman of the Carnegie Institution of Washington's division of plant biology, Stanford, Calif., and professor (honorary) in the department of chemistry at Stanford University, died on 21 June. Born in Chicago in 1885, he received his B.S. degree from the University of Chicago in 1906 and his Ph.D. in 1909. The following year he was appointed a staff member of the Carnegie Institution's Desert Laboratory at Tucson, Ariz., where he remained until 1920 when he moved to the Institution's Coastal Laboratory at Carmel, Calif. In 1928 he became chairman of the newly-created division (now department) of plant biology, which was established on the Stanford University campus in 1929. For a year he was director of the natural sciences division of the Rockefeller Foundation in New York, but in 1931 resumed his previous post.

Dr. Spoehr's scientific interests centered on the formation of organic matter by photosynthesis in plants, and he was one of the first scientists in the United States to investigate seriously the process of photosynthesis. His book, *Photosynthesis* (1926) is used by biologists and biochemists throughout the world. He made numerous investigations in pure carbohydrate chemistry, and in the occurrence and interconversion of carbohydrates in plants during respiration and photosynthesis. He was deeply concerned with the eventual application of basic research in photosynthesis to increasing the world's food supply, and this concern led him to seek modification of the plant's composition by changing its environment—specifically to increase the protein and fat content of algae at the expense of the carbohydrates. This undertaking contributed greatly to the recent rapid development of large-scale cultures of algae for use as food.

Dr. Spoehr's scientific eminence was recognized by election to membership in the American Philosophical Society, the American Academy of Arts and Sciences, and honorary membership in the Linnean Society of London and the Deutsche Botanische Gesellschaft of Berlin. The University of Chicago conferred on him

an honorary doctor of science degree in 1929 and gave him one of its Distinguished Alumni Awards in 1943. He was active in a number of learned societies and served as vice president of the American Society of Naturalists in 1946; president of the American Society of Plant Physiologists, 1944–45; and president of the Pacific Division of the AAAS, 1951–52.

Scientists in the News

Harvey S. Allen, associate professor of surgery in the Northwestern University medical school has received a Fulbright grant to lecture on hand surgery for 3 mo next year at the Society and Home (for cripples), Copenhagen, Denmark.

Wade Thomas Batson, assistant professor of biology of the University of South Carolina, is on leave of absence to serve as assistant in the university relations division of the Oak Ridge Institute of Nuclear Studies. He will assist **W. W. Grigorieff,** chairman of the division, in carrying out Institute programs of particular interest to universities.

For his work on photographic emulsions, **Burt H. Carroll** of Kodak Research Laboratories has been granted the Henderson award of the Royal Photographic Society of Great Britain. The award, a bronze medal and a small sum in cash from an endowment, is made "for the most useful discovery in or essay on photographic chemistry."

Edmund Claxton of the Armstrong Cork Co., Lancaster, Pa., was chosen vice president and the following were appointed to the board: for 3 yr, F. Stuart Fitzpatrick, H. N. Huntzicker, Thomas D. Jolly, J. W. Kreuttner, Harry C. Plummer, R. A. Smith, and P. J. Walker; for 2-yr terms to fill vacancies, Robert W. Cutler, and Mr. Claxton; for 1-yr terms to fill vacancies, H. A. Leedy and Clarence A. Thompson.

The Triennial research award of Iota Sigma Pi, national chemical honorary society for women, has been presented to **Donna B. Cosulich,** senior research scientist at Bound Brook Laboratories of the American Cyanamid Co.

Bjorksten Research Laboratories, Inc., has announced the appointment of **George D. Creelman** as technical service director. Formerly with M. A. Hanna Co., Cleveland, he will act as liaison between the technical staff at Madison and clients sponsoring research programs with the organization.

Jacob P. Den Hartog has been appointed head of the department of mechanical engineering at the Massachusetts Institute of Technology, where since 1945 he has been in charge of the division of applied mechanics. He is an authority in the field of mechanical vibrations, and during World War II served with the U.S. Navy Bureau of Ships. Born in Ambarawa, Java (Indonesia), he became a naturalized U.S. citizen in 1930.

Charles L. Dunham, chief of the medical branch in the U.S. Atomic Energy Commission's division of biology and medicine since 1949, has been appointed deputy director of the division. He will assist John C. Bugher in the administration of the commission's biomedical program, which includes activities in the fields of medicine, biology, agriculture, genetics, biophysics, radiation instrumentation, and technical aspects of civil defense.

Cornell University has announced the appointment of **John L. Finan** as a visiting professor of psychology for the fall term. Since 1951 he has been assistant director of the Army's Human Resources Research Office at George Washington University. He will offer two courses at Cornell, on the psychological basis of social behavior and on physiological psychology.

Fred M. Hauserman, of E. F. Hauserman Co., Cleveland, has been elected president for 1954–55 of the Building Research Institute, a branch of the Division of Engineering and Industrial Research, National Academy of Sciences–National Research Council, Washington, D.C.

Thomas Hindle has been appointed assistant dean of the Temple University Medical School. A graduate of the school, he recently completed his internship at the university hospital.

The University of Maryland has appointed **S. B. Jackson** professor of mathematics and head of the department of mathematics.

Robert Jastrow, formerly assistant professor of physics at Yale University, has been appointed to the staff of the nucleonics division of the Naval Research Laboratory, Washington, D.C.

The applied physics division at the Midwest Research Institute has named **Sheldon L. Levy** manager. Dr. Levy, formerly mathematics professor at Brown University, succeeds **R. R. Hancox,** who is now with the Great Lakes Pipeline Co.

Robert M. McAmmond has been appointed chief of the New York Department of Mental Hygiene's newly created office of planning and procedure.

Ernest E. McCollough, Cumberland, Md., will go to Judson College, Marion, Ala., this fall as chairman of the division of sciences and professor of chemistry and physics. Previously associated with the Celanese Corp. of America as a research chemist, he is replacing **H. C. Steele** who is retiring from his duties as head of the science division.

George A. Miller has been appointed associate professor of psychology at Harvard University effective 1 Feb. 1955. Dr. Miller, who is now on the faculty of Massachusetts Institute of Technology, was one of the group that worked, during and after World War II, to perfect methods of assuring communication by voice against a background of noise and mechanical distortion such as occurs often in military and naval action.

V. Lawrence Parsegian is resigning as director of the research division, New York operation office, U.S. Atomic Energy Commission, effective 1 Sept., to accept appointment as chairman of the engineering group and professor of nuclear engineering at Rensselaer Polytechnic Institute. The engineering group comprises seven degree-granting engineering departments with an enrollment of more than 2000 students.

Henry B. Sargent, president and general manager of the Arizona Public Service Co., Phoenix, has joined Stanford Research Institute's Board of Directors.

Six authors of outstanding technical papers published by the American Society for Testing Materials have been honored.

Clyde E. Work and **Thomas J. Dolan,** University of Illinois, "The influence of strain-rate and temperature on the strength and ductility of mild steel in torsion," Charles B. Dudley medal.

A. A. Wagner, Bureau of Reclamation, Denver, "Lateral load tests on piles for design information," C. A. Hogentogler award.

E. T. Wessel and **R. D. Olleman,** Westinghouse Electric Corp., "Apparatus for tension testing at subatmospheric temperatures," Richard L. Templin award.

John T. Richards, Penn Precision Products, Inc., "The corrosion of beryllium copper strip in sea water and marine atmospheres," Sam Tour award.

In addition, two ASTM awards established this year to honor Max Hecht and Frank E. Richart were given, respectively, to **Max Hecht,** Power Stations Chemistry, Drexel Hill, Pa., for the study of water as an engineering material, and to **Albert T. Goldbeck,** National Crushed Stone Association, Inc., Washington, D.C., for contributions in the field of concrete and concrete aggregates.

Meetings

The program of the 62nd annual meeting of the **American Psychological Association,** which will be held in New York, 3–8 Sept., appeared in the July issue of *The American Psychologist*. At the various sessions some 6000 members of APA will meet to hear discussions of approximately 50 subjects ranging from child psychology to desegregation, problems of old age, industrial relations, psychological warfare, and related topics. For further information write to APA headquarters, 1333 16th St. NW, Washington 6, D.C.

The National Association of Biology Teachers has received a grant of $15,000 from the National Science Foundation to conduct a work **conference on the improvement of biology teaching** in colleges and high schools at the University of Florida, 28 Aug.–6 Sept. Richard L. Weaver of the University of Michigan and Samuel Meyer of Florida State University are serving as codirectors of the conference and are selecting the 90 delegates, largely from the 10 southeastern states.

The conference is being held in conjunction with the annual meeting of the American Institute of Biological Sciences and one summary session will be held the evening of 6 Sept. so that those attending AIBS meetings may hear the recommendations of the conference.

"Gravity day" will be held at New Boston, N.H., on 28 Aug. In the morning Roger W. Babson, founder of Gravity Research Foundation, will speak on "Why does our world revolve?" In the afternoon there will be discussion of problems concerning gravitation, and the 1953 winning essays on gravity will be considered.

At the 35th summer meeting of the **Mathematical Association of America** at the University of Wyoming, 30–31 Aug., L. H. Loomis of Harvard University will deliver the third series of Earle Raymond Hedrick lectures on the topic "Convex sets." These lectures, named in honor of the first president of the association and delivered annually at its summer meeting, are a series of three expository lectures on a subject of current interest in mathematics.

On 7 Sept., during the annual meeting of the American Institute of Biological Sciences, Gainesville, Fla., the Institute's Publications Committee is sponsoring a special **symposium on the communication of research results.** John A. Behnke, associate administrative secretary of AAAS, assisted in organizing the following program, which will be under the chairmanship of James Bonner of the California Institute of Technology: "Introduction: a blueprint for streamlining biological journal publication," William Duryee, National Cancer Institute, and chairman, Publications Committee, AIBS; "Better preparation of material," Richard M. Hewitt, senior consultant, Division of Publications, Mayo Clinic, and assistant professor of medical literature, Mayo Foundation; "Modern reproduction of material," Robert Bray, deputy chief, Technical Information Division, Library of Congress; "Indexing and rapid differential selecting of material," Ralph Shaw, director of the library, U.S. Dept. of Agriculture; "The use of material," Ralph Cleland, professor of botany, Indiana University.

Society Elections

American Association of University Professors: pres., William E. Britton, University of Illinois; 1st v. pres., Robert L. Calhoun, Yale University; 2nd v. pres., Harold Newton Lee, Tulane University; general sec., Ralph E. Himtead; treas., Florence P. Lewis, Goucher College.

American Board of Clinical Chemistry: pres., Otto A. Bessey, University of Texas School of Medicine; v. pres., A. E. Osterberg, Abbott Laboratories, N. Chicago; sec.-treas., O. H. Gaebler, Henry Ford Hospital, Detroit.

American Society for Experimental Pathology: pres., Russell L. Holman, Louisiana State University Medical School; v. pres., Harold L. Stewart, National Cancer Institute; sec.-treas., Cyrus C. Erickson, University of Tennessee College of Medicine.

Medical Library Association: pres., Wilma Troxel, University of Illinois Medical School; v. pres. and pres.-elect, Wesley Draper, Medical Society of the County of Kings and Academy of Medicine of Brooklyn; honorary v. pres., E. H. Cushing, Washington, D.C.; sec., Esther Judkins, Rockefeller Institute for Medical Research; treas., Pauline Duffield, State Medical Association of Texas.

Education

On 23 Sept. from 6:00 to 7:00 P.M., E.D.S.T., the American College of Physicians will utilize television through a national closed circuit over the Columbia Broadcasting System to carry to its members and their colleagues a "Symposium on the management of hypertension." This telecast is made possible through the cooperation and support of Wyeth Inc. of Philadelphia, and will be the **first nationwide telecast for postgraduate medical education.**

The panel of physicians who will participate includes Cyrus C. Sturgis of the University of Michigan; F. H. Smirk of the University of Otago (New Zealand); Garfield G. Duncan of Pennsylvania Hospital, Philadelphia; R. W. Wilkins of Massachusetts Memorial Hospital, Boston; and Edward D. Freis of Georgetown University.

Harvard University this fall will start to train graduate students in the field of **data processing.** A specialized group will be selected as candidates for the new M.S. degree, the first such to be offered in the United States. Data processing involves the use of automatic computing machinery for problems where storage and handling of large amounts of information are required.

In business, its aim is the automatic office, with customer billing and inventory control done entirely without human aid. Life insurance companies, large retail stores, and public utilities are believed to be among those that could use digital computers to great advantage. In industry, data processing looks toward the day of the automatic control of factory operations. Chemical and oil industries have already made a start toward automation in this field.

The following is the schedule for the **Northwestern University lecture series,** "New methods of physical chemistry," to be given on the downtown Chicago campus on Tuesday evenings. For further information write to Dr. R. G. Pearson, Chemistry Department, Northwestern University, Evanston, Ill.

28 Sept., "Ionic properties of polyelectrolytes," F. T. Wall, University of Illinois; 5 Oct., "Isotope fractionation studies applied to chemical and geochemical problems", J. G. Thode, McMaster University, Canada; 12 Oct., "Kinetic methods for rapid chemical reactions", R. P. Bell, Oxford University, England; 19 Oct., "Structural and kinetic applications of infrared spectroscopy", Bryce Crawford, Jr., University of Minnesota; 26 Oct., "Shock and detonation waves as a research tool", G. B. Kistiakowsky, Harvard University; 2 Nov., "Applications of physical chemical methods to the semiconductor field", C. S. Fuller, Bell Telephone Laboratories; 9 Nov., "Chemical applications of nuclear magnetic resonance", R. A. Ogg, Jr., Stanford University; 16 Nov., "Recent developments in the application of magnetochemistry to the study of catalysts", P. W. Celwood, Northwestern University; 23 Nov., "Paramagnetic resonance studies of free radicals produced by radiation", R. Livingston, Oak Ridge National Laboratory; 30 Nov., "X-ray structure determinations by means of the x-rac", R. Pepinsky, Pennsylvania State University; and 7 Dec., "Some physical methods of studying aerosols", F. T. Gucker, Jr., University of Indiana.

Fellowships and Awards Available

Nominations are solicited for the 1955 **Borden award in nutrition** made available by the Borden Company Foundation, Inc. The American Institute of Nutrition will make this award in recognition of distinctive research in the United States and Canada that has emphasized the nutritive significance of the components of milk or of dairy products. The award will be made primarily for the publication of specific papers during the previous calendar year, but the jury of award may recommend that it be given for important contributions made during the past several years. Membership in the American Institute of Nutrition is not a requisite of eligibility for the award. Employees of the Borden Company are not eligible.

Nominations, accompanied by supporting data, *must be submitted by 1 Jan.* to W. D. Salmon, Animal Husbandry and Nutrition, Alabama Polytechnic Institute, Auburn, Ala.

The **Committee on Disaster Studies** of the National Research Council in its last meeting emphasized the need to encourage research by competent representatives of the social sciences and related disciplines who wish to advance knowledge in their own fields and contribute to the solution of disaster problems. The Committee is interested in the effects of disaster upon individuals, groups, communities, and societies; human response to the threat and impact of disaster, ranging from the individual to the national level; the human aspects of such problems as communications, warning, organization, rescue, welfare, medical care, evacuation, and logistics; and the long-term effects and recovery problems of disaster.

The Committee can support this development to a limited extent by providing financial assistance for investigations and analyses. Assistance will be similar to grants-in-aid and ordinarily will range from $200 to $2000. Projects requiring larger sums will be considered if they are especially meritorious and pertinent. Proposals from graduate students and other qualified investigators will be entertained. These should reach the Committee's offices at 2101 Constitution Ave., Washington 25, D.C., *by 1 Sept.*

A new annual **scholarship in American studies** valued at $600 has been established at New York University's

Graduate School of Arts and Science, beginning with the 1954–55 academic year. A gift of Daniel Lerner, professor of sociology at the Massachusetts Institute of Technology, and his wife, the study grant honors Dr. Lerner's father, the late Louis Lerner.

Applications for **U.S. Government awards under the Fulbright Act** for the academic year 1955–56 *must be postmarked no later than 15 Oct.* The awards offered are for university lecturing and for research at the postdoctoral level in Europe and Asia. For detailed information, address the Conference Board of Associated Research Councils, Committee on International Exchange of Persons, 2101 Constitution Ave., Washington 25, D.C.

Grants and Fellowships Awarded

The first three fellowship awards of $2000 each for teaching and study at the Columbia University Institute of **Air Flight Structures** have been announced jointly by John A. Krout, vice president and provost of Columbia, and Harry F. Guggenheim, president of the Daniel and Florence Guggenheim Foundation. Winners of fellowships are Jerome L. Sackman, Oscar W. Dillon, Jr., and Richard P. Shaw. Purpose of the Institute, formed in January on a grant from the Daniel and Florence Guggenheim Foundation, is to train exceptionally qualified graduate students in the comparatively new field of air flight structures and to conduct research in aircraft design and structure.

A research grant from the **American Philosophical Society** is enabling A. E. Porsild, chief botanist of the National Museum of Canada, Ottawa, to carry out extended studies of the taxonomy and distribution of arctic plants. He has sailed for Europe where he will visit some of the leading herbaria and libraries.

The **Atlantic Refining Co.**, Philadelphia, has announced the names of the winners of the 2 fellowships and 12 scholarships granted to colleges and universities for the 1954–55 academic year. The awards are made for the purpose of encouraging and assisting outstanding undergraduate and graduate students who show the greatest promise of success in the fields of science, engineering, and research directly related to petroleum industry operations.

Fellowships

H. A. Deans, Rice Institute. Chemical engineering.
R. C. Reynolds, Washington University. Geology.

Scholarships

R. A. Moses, Alabama Polytechnic Institute. Chemical engineering.
R. O. Barnes, Colorado School of Mines. Geophysics.
R. S. Johnson, Georgia Institute of Technology. Electrical engineering.
B. A. Dalton, University of Kansas. Petroleum engineering.
K. H. Ault and J. R. Crocker, Louisiana State University. Petroleum engineering.
W. H. Thompson, University of Oklahoma. Petroleum engineering.
T. V. McEvilley, St. Louis University. Geophysics.
J. B. Ashby, Southern Methodist University. Geology.
G. W. Millsap, Texas A. & M. College. Chemical engineering.
J. Medford, Texas Technological College. Mechanical engineering.
L. P. White, University of Texas. Geology.
M. J. Hagan, Jr., University of Tulsa. Petroleum engineering.

Two fellowship awards given annually by the **Educational Testing Service,** a national nonprofit testing agency, for graduate study in psychology at Princeton University have been announced. The recipients are Robert F. Boldt, Fremont, Nebr., and Donald P. Estavan, Redwood City, Calif. The award is $2500 annually for each fellow.

The Carnegie Corp. of New York, through a grant to ETS, has made it possible to extend for a second year the visiting psychometric fellowship to John A. Keats, a graduate of the University of Melbourne and a member of the staff of the Australian Council for Educational Research in Melbourne. Announcement also is made by ETS of the reappointment as psychometric fellows of Norman Cliff, Bertram Karon, Anton Morton, and Robert Sadacca.

The American Heart Association's second annual **Howard W. Blakeslee awards** for outstanding reporting in the field of heart and blood vessel diseases will be presented on 14 Sept. to Cathy Covert, medical writer, and Arthur Cornelius, chief photographer, of the Syracuse *Herald-Journal,* for their series of ten articles on heart diseases that appeared in Dec. 1953; Clive Howard of Ridgewood, N.J., for his article, "Can heart disease wreck your marriage?", in the Feb. 1953 issue of *Woman's Home Companion*; "American inventory," for "The mechanical heart," a documentary television program, telecast on NBC-TV from Harper Hospital, Detroit, 15 Feb. 1953; and William A. Brams, of Chicago, Ill., for his book, *Managing Your Coronary* (Lippincott, Philadelphia, 1953). Each award involves an honorarium of $500.

Vladimir Nikolaevich Ipatieff, the chemist responsible for many significant developments in chemistry, including an inexpensive method for making the raw material leading to mass production of synthetic rubber, has been honored by the formation of an **Ipatieff Gift Fund** for the John Crerar Library of Chicago. The fund of $5000 is a joint bequest from Dr. Ipatieff's estate and an anonymous donor. It will be used to purchase books on chemistry for the library, a nonprofit institution, open to the public, whose collection is devoted entirely to science and technology.

M. Truman Fossum, agricultural economist in the U.S. Department of Agriculture, has received the **Norman Jay Colman award** for 1954 from the American Association of Nurserymen in recognition of his efforts directed toward the development of a sound program of economic research for florists and nurserymen, and for his *Trade in Horticultural Specialties, a Statistical Compendium,* published by the USDA in 1953. It is the first award to be given by the association in recognition of economic research in ornamental horticulture. Last year, Mr. Fossum received an award from the Foundation for Floriculture of the Society of American Florists.

Miscellaneous

The American Southwest is featured in the August issue of the ***American Anthropologist,*** journal of the American Anthropological Association. This marks the first time in the history of the 66-yr-old publication that an entire issue has been devoted to a single area. Sol Tax of the University of Chicago is editor of the journal, but Emil W. Haury, American Indian specialist of the University of Arizona, was guest editor for the special issue. Single copies may be obtained for $2.25 from the Executive Secretary, American Anthropological Association, Box 71, Andover, Mass.

The following **chemicals** are wanted by the Registry of Rare Chemicals, Armour Research Foundation of Illinois Institute of Technology, 35 W. 33 St., Chicago, Ill.: potassium thioplatinate; dilauryl selenide; tetraphenylgermanium; zinc hydride; potassium monoxide; truxillic acid; 3,3,3-trichloropropene; 1,2,3-butanetriol; tri(p-nitrophenyl)carbinol; 2,3,5,6-tetramethylbenzoic acid; succindialdehyde; piperidine-4-acetic acid; 4-nitrohydrindene; 2,4-dichlorobenzyl alcohol; n-laurylpiperidine; chroman-5,6-quinone; phthalazone; scyllitol; cymarin; gamma-tocopherol.

The Bavarian State's **Museum of Ethnology** in Munich was reopened early in July. Some 12 yr ago its collections were evacuated to safeguard them from war damage. Since the reopening, ethnological treasures from all parts of the world are being shown in alternating exhibits in 12 halls of the museum's east wing. The original "Ethnographical Collection" dates from 1817; it was established as an independent museum in 1868.

Abstracts of 29 papers presented at a symposium on **neurosecretion,** held in Naples last year were recently printed in Italy in *Pubblicazioni della Stazione Zoologica,* Vol. 24, Supplemento, Convegno Sulla Neurosecrezione. Participants in the symposium came from the United States, Denmark, England, France, Germany, Italy, Japan, and Sweden.

A preliminary hearing was held recently to explore the possibility or advisability of developing a uniform system for use in coding biological taxonomic entities, since it is known that several laboratories have already established their own punch-card records. Participants at this exploratory meeting were from the Library of Congress, the U.S. Department of Agriculture, the Smithsonian Institution, and the Chemical-Biological Coordination Center of the National Research Council. To facilitate the exchange of information between various laboratories, it would seem to be highly desirable for research groups to use a uniform **taxonomy coding system.** If the need for uniformity is confirmed by a significant number of biologists, a start on the formation of a standardized code should be made as soon as possible.

The immediate problem is to determine what areas of biology could be usefully served by such a code. It is requested that those who have devised or adopted a system for coding taxonomic entities, or who may be conducting work which might benefit from such codification, submit their opinions concerning a standardized biological taxonomy code to Dr. G. Congdon Wood, Chemical-Biological Coordination Center, National Research Council, 2101 Constitution Ave. NW, Washington, D.C.

New Periodicals

Eugenics Quarterly, vol. 1, No. 2, June 1954. Helen G. Hammons, Ed. American Eugenics Society, 230 Park Ave., New York 17. Quarterly. $3 per year. Successor to *Eugenical News.* . . . *Composite Wood.* vol. 1, No. 3, Apr. 1954. D. Narayanamurti, Ed. 15 Beeson Rd., New Forest P.O., Dehra Dun, U.P., India. Rs. 14 per year; Rs. 2/8 per issue. . . . *Acta Medica et Biologica.* vol. 1, No. 1, Mar. 1953. Niigata University School of Medicine, Niigata, Japan. . . . *Opera Botanica.* (In English, German, and French.) vol. 1, No. 1, H. Hjelmqvist, Ed. Botanical Society of Lund. Distributed by Almqvist and Wiksell, Stockholm. Irregular. Kr. 30 per vol. Continuation of *Botaniska Notiser, Supplement.* . . . *Acta Cuyana de Ingeniería.* (In Spanish.) vol. 1, No. 1, Jan. 1953. Facultad de Ingeniería y Ciencias Exactas Físicas y Naturales, San Juan, Argentina. . . . *Bulletin of the Central Electrochemical Research Institute Karaikudi.* vol. 1, No. 2, Apr. 1954. A. Narayanaswami, Ed. Central Electrochemical Research Institute, Karaikudi, India. Rs. 12/- per year (foreign, incl. postage); Rs. 2/- per issue. . . . *Eye to Eye.* Bull. of the Graphic History Society of America. No. 3, Dec. 1953. Paul Vanderbilt, Ed. Graphic History Society of America, P.O. Box 4402, Washington, D.C. Quarterly. $10 per year. . . . *The Prescriber.* vol. 1, No. 2, June 1954. Russel V. Lee, Ed. The Prescriber and Prescriptionist, P.O. Box 9189, San Diego 9, Calif. Monthly. $5 per year; 50¢ per issue. . . . *The Prescriptionist.* vol. 1, No. 2, June 1954. Edward P. Fleming, Ed. The Prescriber and Prescriptionist, P.O. Box 9189, San Diego 9, Calif. Monthly. $5 per year; 50¢ per issue. . . . *Industrial Science and Engineering.* vol. 1, No. 1, Jan. 1954. Advanced-student edition of *Industrial Laboratories.* George A. Whittington, Ed. Industrial Laboratories Pub. Co., 201 N. Wells St., Chicago 6, Ill. Monthly. Gratis to senior and graduate students working toward degrees in the engineering sciences. Available to others at $25 per year. . . . *Current Chemical Papers.* No. 1, 1954. Classified world list of new papers in pure chemistry. Cyril Hinshelwood, Ed. The Chemical Society, Burlington House, London, W.1., England. Monthly. $7.50 (post free) or $12.75 (air mail) per year. . . . *Boletín del Instituto de Antropología* (in Spanish). vol. 1, No. 1, Nov. 1953. Universidad de Antioquia, Medellín, Colombia. . . . *Nuclear Notes for Industry.* No. 1. U.S. Atomic Energy Commission, Technical Information Service, Oak Ridge, Tenn. Formerly listed in *Nuclear Science Abstracts* as "Selected Subjects of Interest to Industry."

Book Reviews

Nucleo-Cytoplasmic Relations in Micro-organisms. Boris Ephrussi. Oxford Univ. Press, New York, 1953. vii + 127 pp. Illus. + plates. $3.75.

Embryology and developmental differentiation have long been recognized as subjects with which genetics must eventually make a firm alliance. The history of modern attempts to achieve a synthesis, taking into account the results of both experimental embryology and chromosome investigations, begins in the 19th century. An exhaustive account and penetrating critique of the accomplishments of this period appeared in 1895 in Y. Delage's monumental book [*La structure du protoplasma et les théories sur l'hérédité et les grands problèmes de la biologie générale* (Reinwald, Paris, 1895)], which in some important respects was a generation ahead of its time. During the present century genetics, cytology, and experimental embryology have been intensively cultivated, but relatively little investigative and theoretical activity has been directed toward their synthesis. Yet at no time was this totally neglected. Between 1915 and 1940, it was dealt with in a number of books, such as those of E. G. Conklin [*Heredity and Environment* (Princeton Univ. Press, Princeton, N.J., 1915)], E. B. Wilson [*The Cell in Development and Heredity* (Macmillan, New York, 1925)], J. S. Huxley [*Problems of Relative Growth* (London, 1932)], T. H. Morgan [*Embryology and Genetics* (New York, 1934)], H. S. Jennings [*Genetics* (Norton, New York, 1935)], R. Goldschmidt [*Physiological Genetics* (McGraw-Hill, New York, 1938)], and G. H. Waddington [*An Introduction to Modern Genetics* (Macmillan, New York, 1939) and *Organisers and Genes* (Cambridge Univ. Press, New York, 1940)], In the last decade or two, there has been a notable increase in the amount of attention given to the problem.

Attempts at synthesis have differed fundamentally with respect to the genetic significance ascribed to the cytoplasm. On the one hand, the great majority of geneticists, especially in this country, have agreed with H. J. Muller's [*"The gene as the basis of life," Proc. Intern. Congr. Plant Sci.* **1**, 897 (1929)] view of the nuclear gene as the ultimate physical basis of life and have maintained that genetic functions of the cytoplasm exist but rarely and exceptionally. According to this view, the cytoplasm is

> . . . the moat that guards the hereditary estate from the inroads of the variable environment; the dual highway across which supplies from the outside are conveyed to the nucleus and products of cellular activity are transported to the outside world; the factory in which these cross-currents of materials interact to yield produce for home consumption and for export . . . the cytoplasm is the protector of the genes, their purveyor, their workshop, and the display case in which the products of their activity are shown. [T. M. Sonneborn, "The role of cytoplasm in heredity," *Centennial, AAAS*, 243 (1950)].

Developmental differentiation is therefore traced to the action of nuclear genes alone. Assuming that the initial cytoplasmic organization of the uncleaved egg is a consequence of prior gene activity, schemes may be devised to account formally for progressive developmental divergence of both cells and cell regions.

On the other hand, a relatively small group of geneticists is unwilling to concede that the methods of analytic abstraction, which have demonstrated that the nuclear genes intervene in every activity of the cell and the organism, have excluded the possibility of an equally pervasive participation of cytoplasmic materials with genetic properties. They hold that nucleus and cytoplasm form together an autoreproducing system in which both components have essential and genetic functions. Evidences for this view are drawn mainly, but not exclusively, from studies on plants and microorganisms; and these studies have provided a number of models for possible mechanisms of developmental differentiation. Some of the main discoveries, inferences, and developmental models emerging from recent work on microorganisms are set forth and discussed in this small but important book by Ephrussi, based on three lectures given in 1952 at the University of Birmingham.

Ephrussi starts with the familiar argument that reproduction of diverse tissue cells true to type in tissue culture implies a cytoplasmic basis of these genetic differences on the cellular level, for all the diverse cell types in a metazoan body are alike in the kinds of genes they contain. He then reviews a number of examples in microorganisms in which cells with the same genic constitution manifest persistent diversities owing to cytoplasmic differences. After a brief account of cytoplasmic particles or structures that manifest genetic continuity (chloroplasts, kinetosomes, kinetoplasts, and so forth), he presents more extensive accounts of the genetics of "little colony" in yeast, killers and antigenic types in Paramecium, and the barrage phenomenon in Podospora. Other examples are dealt with only in cursory fashion. This limited survey brings out, however, that a number of diverse physical bases and mechanisms are involved in persistent cell differences. Some involve genetic cytoplasmic particles; others involve persistent "cytoplasmic states." Some are irreversible; others are long-lasting but reversible. All these provide models for developmental differentiation and all illustrate how nuclear genes and the cytoplasm together constitute the underlying genetic system.

One of the chief factual reasons why most geneticists are unwilling to accept such views as being of general validity and applicability is the relative scarcity of the evidence for cytoplasmic inheritance. Ephrussi deals with this difficulty in a penetrating and stimulating addendum, which is one of the outstanding features of the book. It includes two brilliant analyses: (i) of the concept of fundamental character-

istics on the cellular, organismic, and species levels; and (ii) of the significance and limitations of the concept of covariant reproduction.

In the course of the book, Ephrussi refers to the more important alternative interpretations that can be placed upon the facts he discusses, but in so small a book one cannot expect to find them all treated exhaustively and critically. He frankly admits at the start his theoretical bias and conceives his function to be primarily the presentation of evidences and reasons for it. He succeeds admirably in accomplishing his purpose. The book is a clear, informative, lively, and stimulating treatment of a controversial and exceedingly important area of modern biology. It should take and hold an honorable place in the list of books by eminent biologists who have attempted to work toward the synthesis of genetics and embryology.

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Nuclear Theory. Robert G. Sachs. Addison-Wesley, Cambridge, Mass., 1953. xi + 383 pp. Illus. $7.50.

Books on theoretical nuclear physics are not yet numerous, so it is a pleasure to note the appearance of a new one by an eminent and qualified author. Sachs' book is not an elementary one, in the sense that a good working knowledge of quantum mechanics is demanded of the reader. It might, however, be called elementary in the more literal sense that it is concerned with the "elements" or fundamental ideas of nuclear theory. The central unknown in nuclear physics is, of course, the nature of the forces that act between nucleons; they are not like gravitational forces or electromagnetic forces. They are unfamiliar in our experience and are known only by such qualitative aspects, as, for example, that they are intense and of short range. Their nature can be expected to be revealed most directly in the simplest nuclear systems, and in pursuing these basic concepts the author devotes nearly half of his book to a discussion of two-body systems in which a single proton interacts solely with another proton or with a neutron.

In extending the discussion to the many-body problems encountered in more complicated nuclei, Sachs includes a most praiseworthy description of the shell model and the associated quasi-spectroscopic coupling schemes, including in the treatment a discussion of isotopic spin and supermultiplets. This is perhaps the outstanding part of the book. These subjects are confusing to a student who has to dig them out from original research papers, where they have too often been set forth in unnecessarily complicated language. The basic type of treatment given in this book gives one a chance to see the various aspects of the subject placed in coherent relationship.

Other chapters deal with nuclear reactions, the interaction of electromagnetic radiation with nuclei, and beta decay. Few concessions are made to pictorial representation of the matters under discussion. There are not many figures, and experimental data are not woven extensively into the text, although they are adequately referred to in footnotes. Nevertheless, the logic is developed lucidly and the book is well written, so that the advanced student will not find it formidable reading.

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Encyclopédie Entomologique, Catalogue Illustré des Lucanides du Globe. Texte. 223 pp. Illus. ***Encyclopédie Entomologique, Catalogue Illustré des Lucanides du Globe.*** Atlas. 112 plates. R. Didier and E. Séguy. Lechevalier, Paris, 1953. Both volumes, F. 8000.

The Lucanidae, commonly known as stag beetles because the males of many species have enlarged mandibles resembling antlers with which they often engage in combat, have long been favorites with collectors. Other entomologists have attempted to explain the pattern of wide variation in mandible size that occurs among the males of a single species. This new catalog lists nearly 1100 species, most richly represented in southeastern Asia and the East Indies. Only a few dozen species are Nearctic.

The text volume contains general information, indexes, and some illustrations, in addition to the main catalog. The atlas consists of outstanding illustrations, drawn mainly by the master artist Louis Marie Planet. The majority of plates are designed to show the variation exhibited by a single species. Both authors are veteran entomologists at the Paris Museum. Didier has published regularly on Lucanidae since the middle 1920's, while Séguy is best known for numerous major works on Diptera. The last previous world catalog of Lucanidae, in the Junk series, appeared in 1910. In the United States, Bernard Benesh has been the leading modern student of Lucanidae.

This catalog is in a very useful form, with full generic references and the type species of synonymous genera cited. Original references to species are followed by the main subsequent references. A bibliography of about 220 titles is followed by an index of geographic localities, including the catalog numbers of each species recorded from those localities. An index to species, genera, and higher categories is included. One section (pp. 23–61) has notes on various species and descriptions of new species.

This is a well-prepared work of fundamental importance to all serious students of the family. Although the catalog and plates comprise the main contribution, there also are brief sections of a general character, and readers may wish that they had been expanded. For instance, the discussion of geographic matters has relatively few comments on faunistic relationships. In the concise review of important type categories (p. 19), a cotype is defined differently from the meaning attached to it by most modern taxonomists. The authors prefer the term *variety* for an infraspecific category, and they treat *aberration*,

form, race, and *subspecies* as synonymous; this usage is hardly in accordance with the most up-to-date taxonomy. But such details primarily emphasize the desirability of agreeing on terms, regardless of the country in which we work, and they scarcely mar the excellence of this fine systematic contribution.

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Simultaneous Linear Equations and the Determination of Eigenvalues. L. J. Paige and Olga Taussky, Eds. National Bureau of Standards, Washington, 1953. (Order from Supt. of Documents, GPO, Washington, D.C.) 126 pp. Illus. $1.50.

As the proceedings of a symposium, held 23–25 Aug. 1951 at Los Angeles, California, under the sponsorship of the National Bureau of Standards, in cooperation with the Office of Naval Research, this book contains 19 reports. Eight of these reports deal primarily with general methods, procedures, or theories; seven are concerned with special methods or special machines for computing; three involve interpretation or applications to physical or related mathematical fields; one is bibliographical. Nearly all the papers emphasize the development of computing procedures suited to the capabilities of high-speed digital computing machines, in which the effort and time required for input and output are more important than the number or complexity of internal operations. The resulting problems of the degree of approximation of output data are prominent in most of the papers.

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A Symposium on the Mechanism of Enzyme Action. William D. McElroy and Bentley Glass, Eds. Johns Hopkins Press, Baltimore, Md., 1954. xvi + 819 pp. Illus. $11.

This volume, which contains the formal presentations and informal discussions of the Fourth McCollum-Pratt Institute Symposium, maintains the high level of excellence that has characterized this series. The general problem of the mechanism of enzyme action has been considered from a variety of standpoints, each aspect being thoroughly reviewed by experts in the field.

Of particular long-range value to chemists working in this area of biochemistry are the reviews presented on the aspects of enzymatic catalysis that are still in a highly developmental stage. Discussions by Kirkwood, Kauzmann, Eyring, Calvin, Klotz, and others are exceedingly stimulating, because of their frank appraisal of the present state of knowledge of the enzyme as a protein and because they indicate some of the essential pathways of research which must be followed for a clearer understanding of enzymatic catalysis. The volume also contains a valuable series of reviews on the mechanism of electron and hydrogen transport and on the general features of group transfers in enzymatic reactions. These subjects are reviewed in such a manner that this volume should serve as a definitive source of literature for some time, even in fields that move as rapidly as these.

As was the case with the previous volumes in this series, the inclusion of informal discussions with a minimum of editorial modification provides additional expansion of the subjects covered in the formal sections as well as a personal touch of humor and whimsy too frequently absent in the discussions of all-too-serious scientists. Bentley Glass has presented his usual well-sifted summary of the entire symposium.

It seems to me that the scientific value of these symposia and the volumes resulting from them is so nearly self-evident that any comments are unnecessary. Nevertheless, for what one man's opinion is worth, the book is highly recommended to students of biochemistry in all stages of development and should be included on any modern bookshelf in this field.

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Higher Transcendental Functions, vols. I and II. Based, in part, on notes left by Harry Bateman. Bateman Project Staff, A. Erdélyi, Ed. McGraw-Hill, New York–London, 1953. vol. I, xxvi + 302 pp., $6.50; vol. II, xviii + 396 pp., $7.50.

Tables of Integral Transforms, vol. I. Based, in part, on notes left by Harry Bateman. Bateman Project Staff, A. Erdélyi, Ed. McGraw-Hill, New York–London, 1954. xx + 391 pp. $7.50.

The late Harry Bateman projected a definitive compilation of information about, among other things, special functions and definite integrals, and he left an enormous amount of manuscript material on these subjects. The Bateman Manuscript Project was set up in 1948 by the California Institute of Technology, with support from the Office of Naval Research, to continue Bateman's work. It employed four noted specialists —A. Erdélyi, W. Magnus, F. Oberhettinger, and F. Tricomi—and several assistants. It has now produced these magnificent volumes, which should be on the desk of every scientist who ever has to solve any but the simplest differential equation or evaluate any but the simplest definite integral. One more volume of functions and one more of tables are still to appear.

The scope of these books is not as broad as that dreamed of by Bateman (and actually only a small part of his manuscript material could be used), but the books certainly embody the most useful parts of Bateman's plan and present information in a way that is not even approached elsewhere, either in thoroughness or in ease of reference. It will no longer take less time to derive afresh the properties of a special function needed in a particular problem than to search the literature for them.

The volumes on higher transcendental functions form a handbook; proofs are abbreviated or omitted, but definitions and notations are explained in detail, and there are extensive lists of formulas. Functions that already possessed their own treatises are less fully covered than others, but the basic information is always presented, and there are ample references. In volume I, the chapters cover the gamma function and its relatives, hypergeometric functions, Legendre functions, generalizations of hypergeometric functions, and the confluent hypergeometric function. In volume II, Bessel functions, functions of the parabolic cylinder and the paraboloid of revolution, incomplete gamma functions and their relatives, orthogonal polynomials in one and several variables, spherical and hyperspherical harmonics, and elliptic functions and integrals are covered. Each volume has its own subject index and index of notations.

The volume of integral transforms is, in effect, a table of integrals, mostly those involving higher transcendental functions. By choosing the parameters so that, whenever possible, an integral appears in the form of one of the standard integral transforms, the compilers have made the arrangement very convenient for the user. Important integrals which might be written as transforms of more than one type appear accordingly in two or more places. This volume includes Fourier cosine, Fourier sine, Laplace, inverse Laplace, Mellin, and inverse Mellin transforms. The inclusion of both inverse and direct transforms is particularly valuable, since the duplication of this information enables one to use the tables painlessly in either direction, without having to resort to a cumbersome index or to haphazard searching. A self-restraint, as admirable as it is unusual, has led the compilers to use standard notations instead of inventing new, better, and more confusing ones. The definition of the transform under discussion is repeated at the top of each page (another saving of trouble for the user), and all notations are fully explained and indexed at the back of the book.

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Temperature Measurement in Engineering, vol. I. H. Dean Baker, E. A. Ryder, and N. H. Baker. Wiley, New York; Chapman & Hall, London, 1953. 179 pp. Illus. $3.75.

The authors have written a book that will be extremely valuable to the engineer who wishes to use thermocouples for temperature measurement. It will provide him with many specific details that are necessary to devise a temperature-measurement technique that will give accurate and dependable data. This book does not attempt to cover all the details of an innumerable variety of problems, but it does present a comprehensive list of possible techniques, methods of analysis, survey of previous designs, and other information necessary for the development of a well-organized approach to a temperature-measurement problem. Since supplementary reading material is of practical importance to each individual problem, the authors have provided an abundance of reference data.

The book deals primarily with thermocouples because of the superiority that they offer for internal temperature measurement of solids. The early chapters are introductory, discussing temperature and its measurement. Later chapters on thermo-couple-thermometer circuits, indicating instruments, design calculation techniques, installation design types, drilling techniques, special materials, cemented installation designs, and temperature gradient installation designs provide a wealth of detailed information. The clear and concise presentation makes possible the many details without accompanying bulk.

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Advances in Carbohydrate Chemistry, vol. 8. Claude S. Hudson and Melville L. Wolfrom, Eds. Academic Press, New York, 1953. xviii + 408 pp. Illus. $10.

This volume of *Advances in Carbohydrate Chemistry* continues the same format and high quality of the previous volumes. James M. Sugihara, University of Utah, discusses "Relative reactivities of hydroxyl groups of carbohydrates" with respect to reactions involving neighboring group effects, configurational relationships, and selective reactions involved in the etherification, esterification, hydrolysis, and oxidation reactions of carbohydrates.

"The chemistry of the 2-deoxysugars," by W. G. Overend, Pennsylvania State College and University of Birmingham, contains a thorough discussion of the characteristic color reactions, chemical properties, and syntheses of the 2-deoxysugars and their derivatives. With the increasing emphasis recently placed on the importance of deoxyribose nucleic acids, this chapter serves as a background of this aspect of carbohydrate chemistry.

The "Sulfonic esters of carbohydrates" are discussed in a well documented review by R. S. Tipson, Mellon Institute. The chapter, developed in a logical order, starts with a detailed discussion of the preparation of these compounds, their various reactions, and synthetic applications. Wherever possible, attention is called to what appears to be a general type of reaction; however, any known exceptions are mentioned. Many suggestions for future investigations are given.

G. O. Aspinall, University of Edinburgh, presents a summary of the known "Methyl ethers of D-mannose." The physical properties, syntheses, and, in some cases, the isolation of these compounds are discussed.

The inclusion of two chapters dealing with D-glucuronic acid reflects the increasing importance of this compound. In the first of these, C. L. Mehltretter, Northern Regional Research Laboratory, relates recent syntheses of D-glucuronic acid. Special emphasis is given to methods involving the catalytic oxidation of various derivatives of D-glucose. H. G. Bray, Uni-

versity of Birmingham, reviews "D-Glucuronic acid in metabolism" in the second of these chapters. The origin, site, and kinetics of D-glucuronide synthesis are among the topics considered. A comprehensive tabulation of biosynthetic D-glucuronides is included.

T. Mori, Tokyo University, in a chapter entitled "Seaweed polysaccharides," reviews the present state of our knowledge of these compounds, with emphasis on the need for further work in this field. The remaining two chapters consist of a discussion of "The substituted sucrose structure of melezitose," by E. J. Hehre, Cornell University, and a detailed compilation of the "Composition of cane juice and cane final molasses," by W. W. Binkley and M. L. Wolfrom, Ohio State University.

This volume represents a valuable addition to the literature of carbohydrate chemistry.

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Crystal Growth and Dislocations. Ajit Ram Verma. Academic Press, New York; Butterworths, London, 1953. 182 pp. Illus. $5.

One of the most dramatic episodes in the development of our understanding of the nature and significance of imperfections in crystals was initiated by the proposal of F. C. Frank, in 1949, that the presence of screw dislocations could account for the previously baffling growth rates of crystals. Frank's paper was soon followed by Griffin's experimental observation of the predicted growth figures on natural single crystals of beryl. These two papers led to a whole series of studies of spiral growth figures, so that now this field represents one of the major successes of dislocation theory.

In the present monograph, Verma reviews these developments, in which he himself played a major part. In the first two chapters, the author summarizes the problems of accounting for the observed growth behavior of crystals as they appeared before Frank's proposal of the screw-dislocation growth mechanism. In the third chapter, the dislocation concept is introduced, and Frank's growth mechanism is described.

The rest of the monograph is devoted to descriptions of the various experimental methods of observing growth patterns on crystals and of the observations that have been made. So much of this material has been widely scattered in the literature that the present connected account is extremely helpful. The text includes a large number of illustrations from the author's own work, many of which have not been published before.

Crystal Growth and Dislocations fills in a very satisfactory way the need for an account of the studies of dislocations and crystal growth.

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New Books

Elements of Food Engineering. vol. II, *Unit Operations.* Milton E. Parker. Reinhold, New York, 1954. vi + 360 pp. Illus. $8.50.

Medicine and Science. Lectures to the Laity, No. XVI. Iago Galdston, Ed. International Universities Press, New York, 1954. 159 pp. Illus. $3.

Modern Learning Theory. A critical analysis of five examples. William K. Estes *et al.* Appleton-Century-Crofts, New York, 1954. xv + 379 pp. $5.

Linear Transient Analysis. vol. I, *Lumped-Parameter Two-Terminal Networks.* Ernst Weber. Wiley, New York; Chapman & Hall, London, 1954. xiv + 348 pp. Illus. $7.50.

Handbuch der Pflanzenkrankheiten. vol. II, *Die Virus- und Bakterienkrankheiten,* pt. 1, *Viruskrankheiten.* E. Köhler and M. Klinkowski. O. Appel and H. Richter, Eds. Paul Parey, Berlin, ed. 6, 1954. 784 pp. Illus. DM. 150.

The Anatomy of the Migratory Locust. F. O. Albrecht. Athlone Press, London; John de Graff, New York, 1953. xvi + 118 pp. Illus. $6.

Astrophysics: Nuclear Transformations, Stellar Interiors, and Nebulae. Lawrence H. Aller. Ronald Press, New York, 1954. x + 291 pp. Illus. + plates. $12.

Industrial Inorganic Analysis. Roland S. Young. Wiley, New York; Chapman & Hall, London, 1953. viii + 368 pp. Illus. 36s.

Electronics for Everyone. Monroe Upton. Devin-Adair, New York, 1954. xiii + 370 pp. Illus. $6.

Evolution as a Process. Julian Huxley, A. C. Hardy, and E. B. Ford, Eds. Macmillan, New York; Allen & Unwin, London, 1954. 367 pp. Illus. $4.25.

Medical Uses of Cortisone. Including hydrocortisone and corticotropin. Francis D. W. Lukens, Ed. Blakiston, New York, 1954. xiii + 534 pp. Illus. $7.50.

Rare Metals Handbook. Clifford A. Hampel, Ed. Reinhold, New York, 1954. xiii + 657 pp. Illus. $12.

Traité de Génétique. vols. I and II. Ph. L'Héritier. Presses Universitaires, Paris, 1954. 518 pp. Illus. Paper: vol. I, F. 1500; vol. II, F. 900.

Student Personnel Work as Deeper Teaching. Esther Lloyd-Jones and Margaret Ruth Smith, Eds. Harper, New York, 1954. xii + 361 pp. $5.

Isotopic Tracers. A theoretical and practical manual for biological students and research workers. G. E. Francis, W. Mulligan, and A. Wormall. Athlone Press, London; John de Graff, New York, 1954. xvi + 306 pp. Illus. $7.

The Struggle for Existence. Umberto D'Ancona. Trans. by Anne Charles and R. F. J. Withers. Brill, Leiden, Netherlands, 1954. xi + 274 pp. Illus.

Irrigated Soils. Their fertility and management. D. W. Thorne and H. B. Peterson. Blakiston, New York, ed. 2, 1954. xii + 392 pp. Illus. $6.50.

Educators Guide to Free Films. Mary Foley Horkheimer and John W. Diffor. Educators Progress Service, Randolph, Wis., ed. 14, 1954. xiv + 566 pp. Paper, $6.

Archaeology in the Field. O. G. S. Crawford. Frederick A. Praeger, New York, 1953. 280 pp. Illus. + plates. $8.50.

Human Physiology. W. B. Youmans, Macmillan, New York, 1954. xiv + 481 pp. Illus. $6.

Theoretical Physics. Mechanics of particles, rigid and elastic bodies, fluids, and heat flow. F. Woodbridge Constant. Addison-Wesley, Cambridge, Mass., 1954. xiv + 281 pp. Illus. $6.50.

Adhesive Bonding of Metals. George Epstein. Reinhold, New York, 1954. ix + 218 pp. Illus. $2.95.

Miscellaneous Publications

Harvard's View of the Controversy over the Arnold Arboretum. McGeorge Bundy. Arnold Arboretum, Jamaica Plain 30, Mass., 1954. 16 pp.

Instituto de Pesquisas Veterinárias Desidério Finamor. Secretary of Agriculture, Industry, and Commerce, Rio Grande do Sul, Brazil, 1952. 82 pp. Illus.

Les Latérites de Gimbi (Bas-Congo). Série Scientifique No. 60. G. Waegemans. L'Institut National pour l'Étude Agronomique du Congo Belge, Brussels, 1954. 27 pp. Illus. F. 25.

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The Making of Sweden. Allan Kastrup. American-Swedish News Exchange, New York 20. 128 pp. Illus.

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White-Tailed Deer Populations in Illinois. Biological Notes No. 34. Lysle R. Pietsch. Natural History Survey Div., Urbana, Ill., 1954. 22 pp. Illus.

Microlepidoptera of New Guinea, Results of the Third Archbold Expedition. Pt. 3. Verhandelingen der Koninklijke Nederlandse Akademie van Wetenschappen, Afd. Natuurkunde, vol. 49, No. 4. A. Diakonoff. North-Holland Publ. Co., Amsterdam, 1954. 164 pp. Illus.

Prospects for Atomic Power. Sir James Chadwick. Univ. of Toronto Press, Toronto 5, Ontario, 1954. 12 pp. Illus. 75¢.

Annual Report of the Director of the Department of Terrestrial Magnetism, 1952–1953. Carnegie Institution of Washington, Washington 15, 1953. 45 pp. + plates.

Histochemische Methoden. No. 2. Walther Lipp. R. Oldenbourg, Munich, 1954. 24 pp. DM. 6.

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Technical Papers

Use of Three-Component Liquid Systems for Countercurrent Distribution

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If two solutes are to be separated effectively by the countercurrent distribution method without the use of a large number of transfers, the following conditions are necessary: (i) the values of the partition ratios for the two solutes must be sufficiently far apart; (ii) the two partition ratios must not both be too much greater than unity, or both be too much smaller than unity (*1*). Many times a solvent pair cannot be found to meet the second of these requirements when the first has been met. Sometimes in such cases a third liquid component that makes the solvent pair more miscible in one another is added to a system to lower (or raise) both partition ratios. This third liquid component brings both partition ratios nearer to unity, and the three-component solvent system may be satisfactory if there is a composition giving two phases for which the values of the partition ratios of the solutes will satisfy the two afore-mentioned conditions.

It should be pointed out, however, that there are factors other than conditions (i) and (ii) that must be considered in choosing a solvent system (*2*). Also, the importance of conditions (i) and (ii) can be reduced by the use of automatic equipment that makes thousands of transfers practical (*1*). It is the purpose of this note to describe and explain a method for finding the composition of a liquid system of three given liquids that will give the best separation of two given solutes at a given temperature (*3*).

Consider two partially miscible liquids A and B and a third liquid C, which when added to a system of A and B increases their miscibility, thus producing a three-component system with a critical composition of complete miscibility (plait point). This three-component system can, in principle, be represented on the conventional triangular diagram showing a two-phase region with tie-lines joining the pairs of compositions that can exist as phases in contact. Points on the same tie-line are not distinguishable for our purpose, since all such points represent systems having the same two phases and differing only in the relative amounts of these two phases. Our problem, therefore, is reduced to finding the proper tie-line. In most cases the triangular phase diagram and, therefore, the tie-lines are not known beforehand.

Consider any variable α that is in a one-to-one correspondence with the tie-lines. The partition ratios K_1 and K_2 of the two solutes are functions of a single variable α, that is, at a constant temperature. There is an infinite number of ways of choosing α, and these are all equally acceptable in principle, but some are more convenient to use in practice. A convenient choice of α is the volume percentage of C under the condition that the volume of the two coexisting phases be equal or in some other constant ratio. A method of using this choice of α is described here.

When C is added to the system of A and B that has its two coexisting phases in equal volumes, C goes preferentially into one of the two phases, thus causing the volume of this phase to become greater than the volume of the other. Suppose the phase that tends to grow the faster is the A-phase. If C and B are added in the proper ratio, the volumes of the two phases remain equal, and the system follows a path that crosses each tie-line once, and only once, until the critical composition is reached. A determination of K_1 and K_2 at various compositions along this path gives graphs of K_1 and K_2 as functions of α, the volume percentage of C. Both partition ratios are unity at the plait point if the effect of the solute on the system is negligible. The best value of α according to some criterions of separation can now be obtained. Several criterions for effectiveness of separation have been proposed (*1, 2, 4*). Suppose a criterion has been chosen, and according to it the separation S has been expressed as a function of K_1 and K_2. A graph of S as a function of α can then be obtained, and if there is a composition that will give the best separation according to the criterion used, then the graph of S as a function of α should have a maximum at the corresponding value of α. The value of S at that value of α is a measure of the best separation.

It should be noted that paths other than the equal-volume path would give the maximum of S at different percentages of C, but all these percentages correspond to points on the same tie-line.

The advantage of this method results from the fact that the separation is expressed as a function of one variable. The number of experiments required to determine the optimum composition and the best separation possible with a given system is thus reduced to a minimum. Preliminary work in this laboratory dealing with the separation of triglycerides indicates that an estimate of the best composition and the best separation can be obtained from the composition at the plait point and the values of the partition ratios at two other compositions.

It should be noted that the method described here gives the best composition of the solvent system when the two phases have equal volumes. If it is desired to use countercurrent distribution with the volumes of the phases in some other ratio r, then it may be more convenient to obtain the best composition by the use of a path along which the ratio of the volumes of the two phases is kept equal to r.

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9 April 1954.

Isolation of Toxic Crystals from Sweet Peas (*Lathyrus odoratus*)

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Schilling (*1*) has reported the isolation from sweet peas (*Lathyrus odoratus*) of crystals that are active in the production of skeletal changes in rats. Active crystals that appear to be identical to these have been isolated also in this laboratory (*2*). The procedure most recently used in this laboratory is simple and seems to give crystals of good purity.

The first active crystals that I prepared were obtained with the aid of ion-exchange resins. In this isolation, the residue from an alcoholic sweet pea extract was partitioned between ether and water. The aqueous phase was purified by treatment with basic lead acetate followed by passage through the strongly basic anion-exchange Amberlite IRA-400 (hydroxyl form). The toxic factor was then adsorbed on the strongly acidic cation-exchange resin Amberlite IR-105 (H) (*3*), from which it was eluted with 5 percent H_2SO_4. Excess H_2SO_4 was removed with barium hydroxide. After concentration of the solution to a small volume, the addition of alcohol caused the precipitation of an unidentified alkali sulfate, which was removed by filtering the warm solution. Fine, white needles separated on cooling. These sintered and decomposed at about 225°C and consisted of the sulfate of an amine. When they were fed to rats, they gave rise to the typical skeletal changes seen in odoratism (sweet pea lathyrism).

More recently, active crystals have been isolated from sweet peas by means of the procedure used in the following isolation.

Coarsely ground sweet peas (1400 g) were placed in a large Soxhlet extractor and were thoroughly extracted with *n* hexane (Skelly Solve B) to remove lipids. The peas were then dried and extracted continuously with 95 percent ethyl alcohol for 7 hr. The alcoholic extract was allowed to cool and to stand overnight. During this time, dense rosettes of yellowish crystals formed in the extract. These crystals, which represented the impure toxic factor, were purified as follows.

The supernatant solution was decanted, and the crystals were washed several times with ethyl ether to remove small amounts of oily material. The crystals were dissolved in 90 ml of water and were treated with a solution of basic lead acetate until no more precipitation occurred. Following filtration, excess lead was removed with hydrogen sulfide, and the lead sulfide filtrate was evaporated to dryness under reduced pressure. The white, solid residue was dissolved in boiling alcohol with the gradual addition of small amounts of water. On cooling, crystals formed which were filtered with suction, washed with 95 percent alcohol, and dried. The yield was 1.6 g; mp 197°C with decomposition.

Recrystallization from alcohol-water mixtures gave very fine, long, colorless needles melting at 209° to 210°C, uncor. (Fig. 1). The nitrogen content by semimicro-Kjeldahl determination was 21.3 percent (21.25 percent; 21.29 percent) (*4*).

When fed to rats at a level of 0.2 percent of the diet, the crystals were somewhat less effective in producing skeletal changes in the animals than were sweet pea diets containing 25 percent sweet peas.

The crystalline material has the following properties: it is very soluble in water, is insoluble in ether, and has limited solubility in alcohol. It gives a positive ninhydrin reaction. During the isolation studies, it was determined that the toxic factor dialyzes readily through Visking cellulose and that it is not precipi-

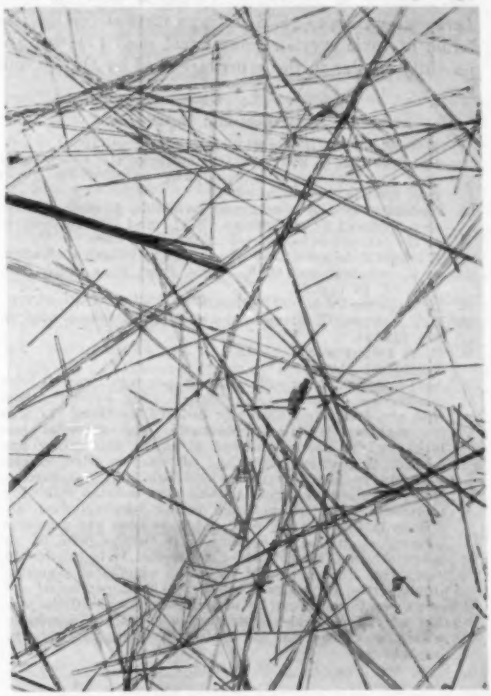

Fig. 1. Toxic crystals isolated from sweet peas (×100).

tated by heavy metal ions (namely, Hg, Pb, Ag, Ba).

The melting point, nitrogen content, and degree of toxicity of the crystals obtained by the latter method indicate that these crystals are identical to those isolated by Schilling (*1*) who reported: mp 193° to 194°C (dec.); nitrogen, 21.1 percent. It would appear that the crystals isolated in this laboratory represent a somewhat higher degree of purity than those reported by Schilling.

The methods of isolation reported in this paper are not suited for the large-scale preparation of the toxic factor from sweet peas, since the yields in terms of percentage of original toxicity are very low. Because of the limited solubility of the toxic factor in alcohol, it is impractical to attempt to extract *completely* the factor from sweet peas with this solvent. However, the extraction with alcohol yields a toxic extract that contains less unwanted material than do the aqueous solvents used by other investigators for extracting *Lathyrus* seeds (*1, 5–7*). The crystallization of the toxic substance directly from the alcohol extract is dependent upon the prior removal of the lipids from the sweet peas. Thus, when the extraction with the Skelly Solve B was inadequate, either no crystals subsequently formed in the alcohol extract, or a difficultly manageable mixture of resin and crystals was obtained.

Addendum. Dupuy and Lee have recently reported the isolation of an active crystalline material from *Lathyrus pusillus* (*8*). Schilling's method for the isolation of toxic crystals from sweet peas (*1*) was apparently similar to the procedure used by Dupuy and Lee.

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9. *Note added in proof*: Since this paper was submitted for publication, Schilling and Strong (*10*) have reported that the compound that was isolated by them (*1*) was β-(γ-L-glutamyl)-aminopropionitrile. The material isolated by the second method given in this paper has proved, through an exchange of samples with Strong (*11*), to be identical to that of Schilling and Strong. However, the toxic crystals that were isolated following treatment with ion-exchange resins (first method described in this paper) could not have been the glutamyl aminopropionitrile, since they were in the form of an essentially neutral sulfate of an amine. It is considered likely that these crystals were the sulfate of β-aminopropionitrile. If this is true, the toxic properties of the sweet pea factor must lie in the aminopropionitrile portion of the molecule. Unfortunately, all the available sulfate was required for toxicity studies. More is in preparation.
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29 March 1954.

Exhaustive Chlorination of Hinokitiol (4-Isopropyltropolone)

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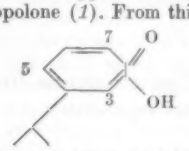
Hinokitiol, isolated from the phenolic part of the essential oil of *Chamaecyparis obtusa* Zieb et Zucc., is 4-isopropyltropolone (*1*). From this structure, it is



seen that it undergoes electrophilic substitution reactions preferably at 3-, 5-, and 7-positions (*2, 3*). Thus when it is chlorinated, for example, there will be three isomerides each of mono- and di-, and one of trisubstituted products. Nozoe, Sebe and associates obtained three monochlorohinokitiols (5-, mp 118.5° to 119.5°C; 7-, mp 47.5° to 48.5°C; 3-, mp 46.5° to 47.5°C (*4*) and three dichlorohinokitiols [3,5-, mp 81° to 82°C (*4*); 3,7-, mp 125° to 126°C (*5, 6*); 5,7-, mp 103° to 105°C (*5*)]. But trichlorohinokitiol has not been reported.

The exhaustive chlorination of hinokitiol gave the trichloro-compound, being isolated as sodium salt.

Through two wash bottles containing concentrated sulfuric acid and a flowmeter, chlorine gas was introduced at a constant velocity of 170 ml/min into a solution of hinokitiol (30.8 g) in glacial acetic acid (200 g) under mechanical stirring, until 5 mole equivalents of chlorine had been absorbed. The reaction mixture was worked up, a large amount of acidic oily products was removed, and the trichloro-compound was obtained from the phenolic portion in the form of sodium salt. After recrystalization from ethanol, the sodium salt melted at 232° to 233°C (decomposition). Analysis for $C_{10}H_8O_2Cl_3Na$—calculated: C, 41.48; H, 2.78; Cl, 36.74; found: C, 41.22; H, 2.88; Cl, 36.96.

Chlorination in an acetic acid (200 g) solution of hinokitiol (30.8 g) at 7°C over a period of 5 hr produced saturation.

Subtracting 1.2 mole equivalents (17 g) that were absorbed by the solvent under the experimental conditions, 5 mole equivalents reacted with hinokitiol.

Nozoe *et al.* (*1*) reported that it is difficult to obtain monochloro-compound when hinokitiol is chlorinated with only 1 mole equivalent of chlorine, the products being always contaminated by some dichloro-compounds, whereas monobromo-compound is obtained in a good yield. Chlorination in an acetic-acid (200 g) solution of hinokitiol (30.8 g) at 7°C during a period of 5 hr produced saturation. When the reaction mixture saturated with 6.0 mole equivalents of chlorine was allowed to stand at room temperature without a stopper, a loss of about 4 mole equivalents of chlorine was noted, hydrogen chloride being liberated.

We wish to thank T. Nozoe and E. Sebe for their kind advice.

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15 March 1954.

Lysis of Cultures Devoid of Vi Antigen by Vi I Bacteriophage of *Salmonella typhosa*

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The concept that the sites for bacterial receptors involved in antigen-antibody reactions correspond to those that determine phage host interactions was developed by Hadley (*1*) and by Burnet (*2, 3*) for certain *Salmonella* serotypes. Levine and Frisch (*4*) observed that differences in the somatic antigens of *Salmonella* group C could be detected by characteristic phage adsorption behavior. Although there are many examples of striking correlations between phage susceptibility and the distribution of heat-stable agglutinogens in various bacterial groups, it soon was observed that there also were many exceptions. This led Burnet (*3*) to explain these discrepancies in terms of the existence of an intimate relationship between the phage and the antibody surface rather than by the assumption of identical adsorption sites for phage and for antibody.

Craigie and Brandon (*5*) described the isolation of a bacteriophage that was specific for the heat-labile Vi antigen of the typhoid organism. The specificity of certain phages for the Vi form of *Salmonella typhosa* led to the demonstration of phage types of this organism by means of preparations of type II Vi phage (*6*). Several Vi phages have been described that are serologically distinct and differ also in respect to particle size, thermal death point, and lytic activity for Vi forms of *S. typhosa*. They have been tested on a great variety of salmonellae, shigellae, *Escherichia coli*, and on Vi and W forms of many strains of *S. typhosa* (*6, 7*). So far as we are aware, none of the Vi phages has been shown to lyse any culture that does not contain Vi antigen, although they are known to attack cultures other than *S. typhosa*. Nicolle *et al.* (*8*) reported that Vi phages lysed *Salmonella paratyphi C* (East Africa), certain cultures of the Bethesda-Ballerup group of paracolons, and cultures described by Kauffmann as *E. coli* (2624-36 and 5396-38).

The object of this report is to present evidence that the specificity of Vi phage I (*6*) is not dependent on the presence of a bacterial component that can be recognized serologically as Vi antigen. This study was initiated as the result of a chance observation of the lysis by typhoid Vi I phage of a culture of *Escherichia freundii* that did not contain Vi antigen. Examination of additional cultures of this species and of their slow lactose-fermenting analogs (*9*) (Bethesda-Ballerup paracolons) revealed that this was not a rare occurrence. Table 1 shows the relationship that exists in these cultures between susceptibility to typhoid Vi I phage and the presence of Vi antigen. The cultures that contained Vi antigen but were unaffected by the phage must be subjected to a more critical examination before it can be stated unequivocally that they are resistant.

The nature of the host-virus relationship in these cultures that appeared to lack Vi antigen was studied along the following lines: (i) comparison of the specificity and serologic nature of Vi I phage propagated on *E. freundii* and on phage type F_1 of *S. typhosa*, and (ii) demonstration of the absence of Vi antigen in certain cultures of *E. freundii* and paracolon bacteria that were lysed by the typhoid Vi I phage. The former was accomplished by the propagation of typhoid Vi I phage on a Vi negative culture of *E. freundii* through four single plaque passages. The starting material was a preparation of Vi I phage that had been propagated on phage type F_1 of *S. typhosa*. This material had been prepared in the Central Enteric Reference Laboratory under the direction of A. Felix and was dated July 1948. The stock of Vi I phage that had been propagated on *E. freundii* 10 was tested in parallel with the Vi I phage received from England by applying both of these to each of the 32 recognized phage types of *S. typhosa*. The results given by the two phage preparations were identical. Even the weaker lysis of types B3, D4, and M given

Table 1. The relationship between susceptibility to Vi bacteriophage and the presence of Vi antigen in *E. freundii* and related paracolons.

Species	No. of cultures	Action of Vi I phage	Vi antigen	Minimum No.* of O groups represented
E. freundii	9	+	−	4
	5	−	+	5
	16	−	−	9
Bethesda-Ballerup paracolons	5	+	−	3
	2	+	+	1
	6	−	+	2
	41	−	−	28

* Some *E. freundii* cultures possessed O antigens that could not be recognized with the serums available.

by the typhoid Vi I preparation was duplicated by the phage grown on *E. freundii*. Many additional tests of these two phages have failed to produce a single divergent reaction. The serologic identity of these phages was established by reciprocal cross-neutralization tests with standardized serums.

The absence of Vi antigen in a phage-susceptible culture of *E. freundii* and in a paracolon bacterium was adduced from inability to demonstrate its presence in agglutination, immunization, and agglutinin adsorption experiments. Slide-agglutination tests of numerous colonies from each of these cultures, as well as from other similar phage susceptible cultures, were made with typhoid Vi serum and were always negative. One rabbit was immunized with lyophilized organisms of *E. freundii* 10; another received cells of a paracolon culture (92) that had been dried from absolute alcohol. Antigens prepared by either means had been shown previously to be effective in engendering Vi-antibody formation by Vi-containing bacteria. No Vi agglutinin could be demonstrated in these serums either by slide- or tube-agglutination tests using living suspensions of *S. typhosa* (2V and Vi I). Although no Vi antigen could be detected by agglutination and immunization experiments, it was necessary to determine whether the cultures that were susceptible to the Vi I phage had the power to bind Vi agglutinin. For this purpose, three different paracolon strains and one strain of *E. freundii* were employed singly to adsorb a Vi serum prepared with a Bethesda-Ballerup paracolon (107). None of the adsorbing strains was able to reduce the Vi titer of this serum as measured by its ability to agglutinate living broth cultures or *S. typhosa* 2V or Vi I before and after adsorption. The adsorbing strains were fully susceptible to the Vi I phage at the time they were used in the experiment.

The afore-described experiments demonstrate the futility of any attempt to establish an absolute correlation between the presence of any particular antigenic constituent of a bacterial cell and its susceptibility to phage. Phage adsorption is a complex process that may be most easily understood in terms of the complementary ionic atmosphere of the phage particle and the adsorbing surface (*10*). It is quite likely that Vi antigen, represented by the presence of certain chemical groupings at the cell surface, exerts its effect on specificity of Vi phages insofar as it contributes electrostatic configurations favorable for adsorption. Pronounced effects of both Vi and O antigen on the electrophoretic behavior of *S. typhosa* have been reported (*11*). Similar effects were also observed (*12*) in a study of the stability of different forms of the typhoid organism in buffer solutions at various *p*H levels. However, it appears that substances serologically unrelated to Vi antigen may mediate the attachment of Vi phages to the cell. In all cultures of *S. typhosa*, and in at least some cultures of *E. freundii* and related paracolons, phage lysis of Vi+ and phage resistance of Vi– forms in the same culture were observed regularly. Vi antigen appears to condition these cells to lysis by Vi phages.

The present observations have no significance for the routine typing of *S. typhosa* by means of specific Vi phages. They may, however, be quite significant for the problem of distribution in nature of Vi-like substances. There are indications that Vi phages other than phage I may have an affinity for some Vi-negative cultures.

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22 March 1954.

Effects of Destructive Distillation on the Uranium Associated with Selected Naturally Occurring Carbonaceous Substances*

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Little is known regarding the organo-uranium compounds or complexes that may exist in uraniferous coal, shale, or other naturally occurring carbonaceous substances.

During the course of geochemical studies on uraniferous coals (*1*), yields of oil, water, and char were determined by a Fischer assay method (*2*). Because of the nature of this technique, it was difficult to establish with certainty whether volatile uranium compounds had been formed during the course of the retort assay. To investigate this possibility, a number of naturally occurring carbonaceous substances have been subjected to dry distillation in small-scale glass apparatus. Experimental results were evaluated on the basis of material balances using accurate techniques for determining the uranium content of the original substances and of the chars obtained from them. A preliminary search of the literature has revealed no publications regarding the volatilization of uranium from such substances during dry distillation.

This work is part of a program undertaken by the U.S. Geological Survey on behalf of the Division of Raw Materials of the Atomic Energy Commission.

The following samples were chosen to provide a variety of carbonaceous substances; the uranium con-

Table 1. Analyses of substances prior to retorting.

Sample	Moisture (%)	Ash (%)*	Uranium*	
			In ash (%)	In original substance (%)
Chattanooga shale	†	75.5	0.011	0.0083
Subbituminous coal	11.8	11.6	0.012	0.0014
Coal from Chattanooga shale	2.3	1.27	2.58	0.033
Swedish kolm	0.87	20.8	1.83	0.38

* Dry basis.
† Analysis on predried sample.

tents ranged from approximately 0.001 to 0.4 percent.

Chattanooga shale (Upper Devonian). Sample was taken 0.94 to 2.44 ft below top of top black interval, Cannon County, Tenn.

Subbituminous coal. Sample was collected from the upper foot of the Luman No. 1 bed, at its outcrop near the center of sec. 28, T. 24 N, R. 95 W, Sweetwater County, Wyo. Geochemical and mineralogic reports on this coal have appeared (*1, 3*).

Coal from Chattanooga shale. Black, lustrous, brittle organic material, subsequently identified as coal by J. M. Schopf of the U.S. Geological Survey (personal communication), was collected in 1953 by L. C. Conant and T. Kehn, also of the Survey, from an outcrop approximately 15 mi north of Nashville, Tenn. Beds of similar material having a maximum thickness of 0.04 ft are sparsely scattered in the shale averaging 3 to 5 seams per 30-ft core.

Swedish kolm. Lenticular specimens of kolm were collected at Kvantorp, Sweden, in 1951, by Breger.

The following techniques were used to obtain the data shown in Table 1 for the original samples and in Table 2 for the chars obtained from them:

Dry distillation. Samples of approximately 1 g were retorted, using a modification of the procedure suggested by Cuttitta (*4*). The material to be retorted was weighed in an 18- by 250-mm glass-stoppered Pyrex test tube. The lightly stoppered tube was then placed, sloping slightly down toward the stopper, in the tubular electric furnace where the material was distilled for 11 min at 500°C. After the tube was cooled in a horizontal position to prevent contamination of the char by the oil and water distillates, it was scored and broken at a point immediately above the char. The char was weighed and analyzed to determine its uranium content.

Determination of moisture. Weighed samples, approximately 0.5 g, of original material or char were dried in an oven for 2 hr at 105° ± 5°C. Loss of weight was recorded as moisture.

Determination of ash. Dry samples, approximately 0.5 g, were ignited to constant weight in an electric furnace at 800°C. Residual material was calculated as the ash content of the original dry sample.

Determination of uranium. Using the dry ash, the extraction-fluorimetric procedure described by Grimaldi, May, and Fletcher (*5*) was employed without modification.

Uranium balances based on the original samples and on the chars obtained from them are shown in Table 3; uranium contents have been calculated from the data of Tables 1 and 2.

The final column of Table 3 shows recoveries of uranium in the char ranging from 91.4 to 111.9 per-

Table 2. Analyses of chars.

Sample	Moisture (%)	Ash (%)*	Uranium*	
			In ash (%)	In original char (%)
Chattanooga shale	< 0.1	81.9	0.010	0.0082
Subbituminous coal†	2.4	19.0	0.016	0.0030
	2.4	18.8	0.016	0.0030
Coal from Chattanooga shale†	0.3	2.2	2.10	0.046
	0.4	2.4	1.93	0.046
Swedish kolm†	< 0.1	26.1	1.96	0.51
	< 0.1	26.1	1.96	0.51

* Dry basis.
† Duplicate analyses.

Table 3. Uranium balances.

Sample	Sample for distillation (g)	Uranium in sample (γ)*	Char (g)	Uranium in char (γ)*	$\frac{\text{Uranium in char}}{\text{Uranium in sample}} \times 100$ (%)
Chattanooga shale	0.9897	82.0	0.9150	75.0	91.4
Subbituminous coal†	0.9978	16.0	0.6034	17.9	111.9
	0.9858	15.8	0.5928	17.5	111.1
Coal from Chattanooga shale†	1.0019	320	0.6796	310	97.0
	0.9522	305	0.6349	305	100.0
Swedish kolm†	0.9784	3720	0.7811	3960	106.2
	1.0149	3860	0.8097	4130	107.0

* Micrograms.
† Duplicate analyses.

cent. These recoveries are based on a minimum of one ash, two moisture, and two uranium analyses. Since the accuracy of the uranium determination alone is at best ±4 percent (*5*), these analyses are all within the limits of analytic error. It has been found by Cuttitta (*6*) that dry-ashing of the samples discussed in this report leads to no loss of uranium. It is evident, therefore, that destructive distillation of these carbonaceous substances results in no appreciable volatilization of uranium.

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5 April 1954.

Isolation of C^{14}-Labeled DPN and TPN by Paper Chromatography from *Lactobacillus plantarum*

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A number of methods have been developed for the isolation of diphosphopyridine nucleotide (DPN) and triphosphopyridine nucleotide (TPN) (*1–4*). Most of the present methods, however, are rather laborious. Previously, in this laboratory, several attempts were made to obtain C^{14}-labeled DPN from *Torula cremoris* grown in a synthetic medium (*5*) to which was added C^{14}-nicotinic acid. The method of Sumner, Krishnan, and Sisler (*3*) was used to obtain the DPN. Yields were extremely small, and purity of the compound was questionable. During studies of inhibition of spleen diphosphopyridine nucleotidase by nicotinamide, Zatman, Kaplan, and Colowick (*6*) obtained labeled DPN from C^{14}-nicotinamide and unlabeled DPN in the presence of spleen enzyme. The radioactive product was isolated and analyzed by ion exchange and paper chromatography. Although the exchange reaction was essentially 100-percent complete, the method was more involved than the one used in the present study (*7*).

In the process of studying the uptake of C^{14}-nicotinic acid and its amide by *Lactobacillus plantarum* (arabinosus) 17-5 (ATCC No. 8014) and several other organisms, it was found by Woodward and Boone (*8*) that about 50 percent of all the nicotinic acid or its amide present in the medium was adsorbed on the cell surfaces. Fifty percent uptake was obtained regardless of the amounts of C^{14}-nicotinic acid or its amide (up to the point of cell saturation) present in the medium and regardless of whether the cells were actively growing or were mature cells suspended in normal saline.

The C^{14} activity on the cells could *not* be removed by several washings with saline and distilled water. It was possible, however, to remove essentially all the radioactive material by repeated washings with *p*H 4 buffer. The primary purpose of this study was to determine whether the labeled material removed from the cell surfaces was unchanged nicotinic acid and/or the amide or some derivative.

Kodicek and Reddi (*9*) described a sensitive technique for the detection of nicotinic acid derivatives by chromatography. This technique was applied to the radioactive material washed from the cells. The use of *p*H 4 buffer as an eluting agent was unsatisfactory because the salt concentration, upon evaporation of the solution, interfered with the chromatography. Suspending the cells in distilled water and adjusting to *p*H 4 was tried and was equally as effective as the buffer for removing the radioactivity without disrupting the cells. Acidic washings were obtained from two groups of cells.

1) "Growing cells." *Lactobacillus plantarum* was grown at 37°C for 18 hr in a modified Snell and Wright medium (*10*) (used for microbiological assays of nicotinic acid) to which had been added 1 μg of C^{14}-nicotinic acid per 10 ml of medium. The labeled nicotinic acid had a specific activity of 4.07 mc/millimole which was equivalent to approximately 43,000 c/min, per 10 ml of medium, when counted in a gas flow proportional counter. At the end of 18 hr the cells were washed twice with 10 ml of 0.85 percent saline and once with distilled water. The cells were then suspended in 10 ml of distilled water, adjusted to *p*H 4, and allowed to stand for 15 min before centrifuging. Control cells treated in the same manner and counted by direct plating showed a C^{14} uptake of about 20,000 c/min. The acid eluate from the cells grown in two tubes of medium was pooled and evaporated to dryness at room temperature. This material was resuspended in 0.5 ml of distilled water. A small aliquot was taken for assay by direct plating, and the remainder (equivalent to about 40,000 c/min) was placed on filter-paper strips for chromatographic analysis.

This procedure was repeated using C^{14}-nicotinamide with a specific activity of 3.51 mc/millimole.

Descending chromatograms were run on the acid eluate from the cells using two solvent systems, n-butanol saturated with water and 60 percent n-propanol. Control samples of known C^{14}-nicotinic acid, C^{14}-nicotinamide, and nonlabeled DPN and TPN were chromatographed along with the acid eluate from the cells. The positions of the known DPN and TPN were located on the chromatograph strips by their characteristic fluorescence under ultraviolet light in the manner described by Kodicek and Reddi (*9*). The positions of the C^{14}-labeled compounds were established by autoradiographs of the filter-paper strips

prepared by placing them in contact with 14 × 17 x-ray film for 7 to 9 days.

The results of chromatographic analysis of the acid eluate from cells grown for 18 hr in the presence of C^{14}-nicotinic acid and amide are summarized in Table 1. Chromatograms of the acid eluate from the cells, using 60 percent n-propanol, showed two bands having R_F values of 0.15 and 0.26. These bands were located both by their radioactivity and by the characteristic fluorescence of DPN and TPN in the presence of ultraviolet light. The R_F values of the radioactive bands and the known samples of DPN and TPN were the same and were identical with those reported by Kodicek and Reddi (*9*) for known compounds of TPN and DPN. No material was left at the point of application, and no other metabolite was found in the acid washes. No traces of any remaining nicotinic acid or nicotinamide could be found in the acid eluate from the cells when either 60 percent n-propanol or n-butanol-water was used to develop the chromatograms. The radioactivity in the cell eluate and the samples of known DPN and TPN showed no movement from the point of application with n-butanol-water. All the radioactive material washed from the cell surfaces was apparently DPN and TPN. The DPN band was more intense and wider than TPN, both in radioactivity and fluorescence.

2) "Resting cells." *Lactobacillus plantarum* was grown in the same manner described in the preceding section except that 1 μg of nonlabeled nicotinic acid or amide was added per 10 ml of Snell and Wright medium. After 18 hr growth, the cells were washed as described in the preceding section and then were resuspended in 10 ml of saline that contained 1 to 2 μg of C^{14}-nicotinic acid or amide. The suspensions were incubated at 37°C for varying intervals of time, 15 min, 1 hr, and 18 hr. After incubation, the cells were washed and the radioactivity was eluted and chromatographed in exactly the same manner as that used for the "growing cells." The amounts of C^{14} activity eluted from the cells incubated for 1 and 18 hr were equivalent to those obtained from cells grown in the presence of the C^{14}-labeled compounds. The cells incubated for only 15 min showed a slightly lower uptake of C^{14} activity.

Table 1. Chromatographic analysis of acid eluate from cells of *Lactobacillus plantarum* grown with C^{14}-nicotinic acid and amide.

Solvent	Material	R_F value
60 percent n-propanol	C^{14}-nicotinic acid	0.72
	C^{14}-nicotinamide	0.84
	Known DPN	0.26
	Known TPN	0.15
	C^{14} cell eluate (2 bands)	0.26 and 0.15
n-Butanol-water	C^{14}-nicotinic acid	0.23
	C^{14}-nicotinamide	0.67
	Known DPN	No movement
	Known TPN	
	C^{14} cell eluate	

The chromatograms of the acid washes from "resting cells" that were suspended in saline containing C^{14}-nicotinic acid and/or amide showed results identical to those from cells grown in the presence of the labeled materials when n-butanol-water was used as the solvent.

When 60 percent n-propanol was used to develop the chromatograms, the acid washes from "resting cells" usually showed only one predominate radioactive band. This band had an R_F value of 0.26, identical with the chromatograph of known DPN and showed the characteristic fluorescence under ultraviolet light. This radioactive band occurred even in the washings from cells that were suspended in the presence of C^{14}-nicotinic acid for only 15 min, indicating that all the C^{14}-nicotinic acid or amide adsorbed on the cell surface was converted to DPN in a few minutes. Occasionally, a faint suggestion of the TPN band could be detected by both radioactivity and fluorescence. This band was not consistent and was extremely faint.

The specific activity of DPN was determined by eluting the labeled material from the chromatogram strips and diluting it to a known volume. A small aliquot of the sample was assayed for C^{14} activity and another for DPN by a modification of the microbiological method of Kohn and Bernheim (*11, 12*) using *Hemophilus parainfluenzae* (ATCC No. 7901). The results showed that the DPN had a specific activity of 3.90 mc/millimole compared with a specific activity of 4.07 mc/millimole for the C^{14}-nicotinic acid, indicating a direct stoichiometric relationship between the specific activity of the nicotinic acid in the medium and the DPN eluted from the cells. This relationship was also true when C^{14}-nicotinamide with a specific activity of 3.51 mc/millimole was used. Preliminary assay of the small amounts of TPN available using the same technique also indicated a stoichiometric relationship between the specific activity of C^{14}-nicotinic acid in the medium and TPN eluted from the cells.

This extremely rapid conversion of C^{14}-nicotinic acid to C^{14}-DPN by cells washed free from the growth medium and suspended in saline plus nicotinic acid indicates that all other moieties of the DPN molecule (phosphate, ribose, and adenine) must already be present in some form in the "resting cell." That an exchange phenomenon between unlabeled DPN and C^{14}-nicotinic acid is involved seems unlikely, since "resting cells" (upon being suspended in saline containing C^{14}-nicotinic acid) convert to DPN 10 to 20 times the amount of nicotinic acid supplied in the medium during their growth phase. Furthermore, the molar specific activity of the C^{14}-DPN, if formed by exchange, would approach only one-half of that of the C^{14}-nicotinic acid.

Quantitatively, 100 μg of C^{14}-nicotinic acid with a specific activity of 4.07 mc/millimole in the presence of 50 to 100 mg dry weight of cells of *Lactobacillus plantarum* (*13*) yielded about 250 to 300 μg of C^{14}-labeled DPN with equivalent molar specific activity.

Some, but not all, of the C^{14} activity remaining in the medium may be recovered by further cell absorption or as C^{14}-nicotinic acid or amide by ether extraction at the proper *p*H.

It is felt that considerable advantage may be offered by this method as a means of obtaining small amounts of pure C^{14}-labeled DPN and TPN with rather high specific activities. No attempt has been made in this preliminary paper to discuss cell surface adsorption phenomena. A discussion of this problem is being prepared by Woodward and Boone (*8*).

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26 March 1954.

Influence of Vitamins upon Incidence of Tumors in tu^{50j} Stock of *D. melanogaster*

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In previous reports, I (*1, 2*) have shown that the penetrance of tumor ^{50j} in *Drosophila melanogaster* is influenced by nutrition. In general, poor nutrition apparently lowers the incidence of tumors in the tu^{50j} stock. Tannenbaum (*3*) and Herskowitz and Burdette (*4*) also have found that poor nutrition and low caloric intake reduces the incidence of tumors.

An excess of several amino acids in the diet (*2*) increased the incidence of tumor in the tu^{50j} stock. This report is concerned with the influence of excessive amounts of vitamins on *D. melanogaster* reared on a rigorously controlled diet (*5*). A vitamin-free and amino acid-free medium (*2*) was inoculated with the yeast *Hansenula anomala,* so that the nourishment of the larva was restricted to the yeast employed. Excessive amounts of various vitamins were added to this medium, and the incidence of tumors produced by a pair of flies in a 10-ml vial was recorded. As the larvae burrow into the medium, some of the vitamins present are taken into the digestive tract.

The influence of the vitamins upon the presence of tumors in tu^{50j} stock of *D. melanogaster* is presented in Table 1. Note that the incidence of tumors is 10.6 percent in the flies reared on the minimal diet. However, significant increases in the tumor production result if the flies are reared on an excessive amount of riboflavin, nicotinic acid, pyridoxine HCl, vitamin B_{12} and p-amino benzoic acid. These vitamins, with the exception of p-amino benzoic acid, are included by Hinton (*6*) in a chemically defined diet of *D. melanogaster.*

Table 1. Tumor incidence in *D. melanogaster* tu^{50j} reared on various mediums inoculated with *Hansenula anomala.*

Added to 1 lit minimal medium		Flies	
Additive	(g)	Total No.	Tumorous (%)
None		2051	10.6
Ascorbic acid	0.333	760	10.1
Riboflavin	1.000	1153	14.8
Nicotinic acid	0.333	732	14.0
Pyridoxine HCl	.333	763	14.1
Calcium pantothenate	.333	781	12.5
Biotin	.333	767	9.1
Inositol	.333	715	10.5
Cholesterol	.500	712	9.2
Ergosterol	1.000	752	9.9
Calciferol	0.500	764	9.5
Vitamin K	.666	700	9.3
Vitamin A	.010	754	9.2
Thiamine HCl	.333	830	9.2
Vitamin B_{12}	.000010	746	21.6
Folic acid	.166	785	10.2
Choline HCl	.166	786	10.3
p-Amino benzoic acid	0.166	777	16.2

It appears that specific vitamins, as well as certain amino acids, in the diet of tu^{50j} stock increase the production of tumors. Thus, the cornmeal-molasses mixture which contains a higher percentage of vitamins and amino acids (*2*) does increase the penetrance of tu^{50j}.

These results present interesting questions that cannot be answered at present: (i) How do vitamins influence tumor production? (ii) Why does an excess of vitamin B_{12} in the diet double the number of tumors in the stock? (iii) Is there a critical amount of nutritional factors in the diet necessary for tumor formation? However, it can be stated definitely that the better the nutrition, the greater the chance of exposing the larvae to nutritional factors that increase the tumor production in tu^{50j} stock of *D. melanogaster.*

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8 March 1954.

A Spectrophotometric Determination of Isonicotinic Acid Hydrazide

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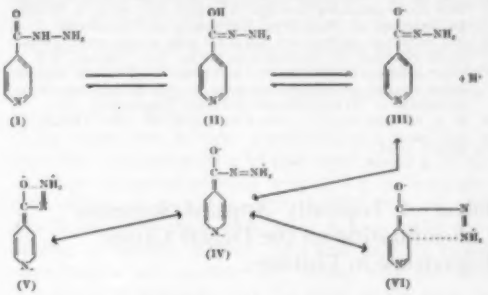
Experiments in this laboratory on the metabolic activities of certain antituberculous drugs necessitated the development of a rapid, sensitive method for the determination of isonicotinic acid hydrazide (INAH) in aqueous solution. Several methods for the determination of INAH and its derivatives have appeared in the recent literature. These methods involve either condensation of isonicotinic acid with CNBr (*1*), condensation of hydrazine with p-dimethylaminobenzaldehyde (*2*) or glutaconic aldehyde (*3*), reduction of ferricyanide by hydrazine (*4*), or measurement of the 265-mμ peak of an isoamyl alcohol extract of plasma (*5*). None of these methods is suitable for the rapid determination of INAH at the level of 1 μg or less per milliliter.

The method described here is based on *p*H-engendered changes in the absorption spectrum of INAH solutions (Fig. 1) In strongly alkaline solutions, a new peak emerges having an extinction coefficient at 298 mμ of 4.8×10^6 cm²/mole (*6*). This peak disappears, reversibly, in acid solution.

Sufficient NaOH is added to an aqueous solution of INAH to bring the final concentration of hydroxide to 0.1*N*. The optical density at 298 mμ of the solution is measured in a spectrophotometer. The lower limit of the method is about 0.5 μg of INAH per milliliter with an over-all sensitivity of about 0.1 μg/ml. The linearity of the concentration curve is shown in Fig. 2.

The effect of *p*H on the absorption at 298 mμ is shown in Fig. 3; the pK_a of the hydrazide is approximately 11. The change in absorption spectrum of INAH in alkaline solution may be associated with the quinoid forms (IV–VI), which are postulated as arising from the enolate ion (III). That the structural



modification causing this change in the absorption spectrum is associated with both an unsubstituted hydrazide group and a free ring nitrogen is demonstrated by the fact that none of the following related compounds (*7*) shows the absorption peak at 298 mμ in alkaline solution: nicotinamide, isonicotinamide, isonicotinic acid, 1-isonicotonyl-2-isopropyl hydrazine, 1-isonicotonyl-2-allyl-2-isopropyl hydrazine dihydrochloride, and N¹-methyl-isonicotinic acid hydrazide (*8, 9*). Substitution of the primary nitrogen may result in steric hindrance preventing the formation of V or VI; substitution of the ring nitrogen could prevent the formation of V. Either of these factors could thus prevent the spectral change associated with free INAH.

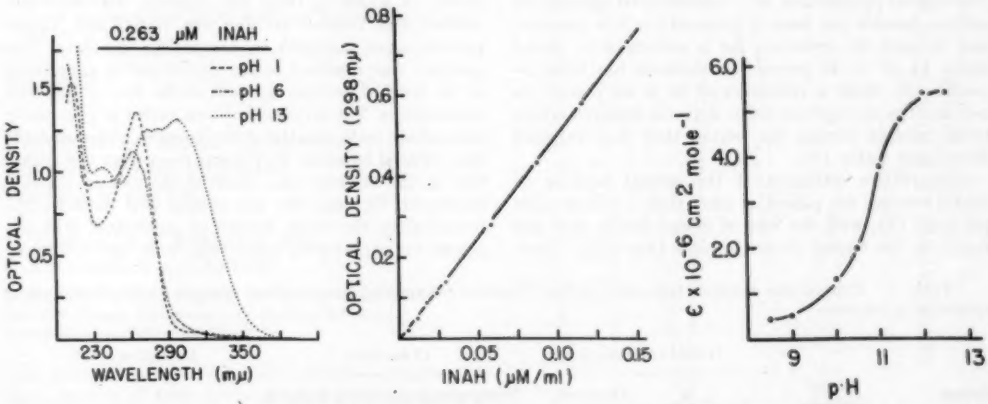


Fig. 1 (left). Effect of the solution *p*H on the absorption spectrum of INAH. Figure is a composite obtained by transcription of three tracings obtained from the Carey recording spectrophotometer. Fig. 2 (center). Concentration curve for the spectrophotometric determination of INAH. Samples were read in 1.0-ml quartz cuvettes in the Beckman spectrophotometer. Fig. 3 (right). Effect of *p*H on the absorption at 298 mμ of solutions of INAH. Solutions containing 0.263 μM INAH per milliliter were adjusted to the indicated *p*H, and the optical density at 298 mμ was measured.

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12 March 1954.

Effect of Topically Applied Stannous Chlorofluoride on the Dental Caries Experience in Children

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At the present time approximately 20 million Americans drink water with a fluorine concentration of approximately 1 ppm or above (*1*). This is nearly one-eighth of the entire population of the United States, but it is probable that at no time will the number ever be more than 50 to 60 percent of the total population. This results from the fact that approximately one-half of the population is served by rural water supplies that are too small to be safely fluoridized. Thus, from a preventive dentistry viewpoint, other effective methods of fluoride therapy must be instituted that will compare favorably with communal fluoridation. The topical application of a concentrated solution of sodium fluoride has been introduced for this purpose, and through its judicious use a reduction in dental caries by 30 to 40 percent in children has been reported (*2*), while a reduction of 50 to 60 percent in new cavities is experienced in 6-yr-old children whose teeth calcified during the period that they ingested fluoridated water (*3*).

Conservative estimates of the annual backlog of dental services are placed at more than 1 billion units per year (*4*), with the cost of dental health care per family in the United States at more than $200 a year (*1*). This comprises 15.6 percent of the nation's entire health bill. It would seem that search should be made for a more effective topical agent.

In an attempt to find a more beneficial compound for use as a topical agent, stannous chlorofluoride (*5*) was applied to the erupted teeth of approximately 800 children, ages 6 to 15 yr, in Gas City, Ind. One-half of the children were treated with a 1-percent aqueous unbuffered solution of sodium fluoride, and approximately the same number received a 4-percent stannous chlorofluoride solution. Both fluorides were applied to the teeth by cotton applicators in a manner similar to that described by Knutson (*6*). This consisted of a thorough dental prophylaxis followed immediately by the first topical fluoride application. Within a period not exceeding 10 days, three additional topical treatments were given, although only the first was preceded by a prophylaxis. The treatment consisted of keeping all surfaces of the teeth moist throughout each 4-min treatment series.

Howell examined all the children in a Mobile Dental Trailer. Excellent light, compressed air, and new dental explorers and mirrors were used. The concentrations of the fluorides used in this study were chosen so that the fluorine levels would be similar. Since an 8-percent stannous chlorofluoride solution was considered unpleasant for use by the children, a conventional 2-percent solution of sodium fluoride could not be used and still maintain equal fluorine concentrations in both solutions. All the solutions were prepared fresh each morning and noon from oxygen-free water (*7*). Approximately 1 yr after the initial fluoride applications, the children were reexamined by the same dentist. At no time did the examiner have any knowledge of which group he was examining or of the previous caries history of the children.

The results of the topical fluoride treatments are shown in Table 1. Only the children who were examined and treated at both the initial and 12-mo periods were included in computing the data. The analysis was confined to the dental caries experience in the erupted permanent teeth at the time of the first examination. The incidence of new caries in previously noncarious teeth treated with stannous chlorofluoride was reduced by about 85 percent more than the reduction in the children who received the sodium fluoride treatment. Through the use of this new fluoride, approximately the same degree of protection was obtained on surfaces in teeth that were noncarious at

Table 1. Comparison between topically applied stannous chlorofluoride and sodium fluoride on the dental caries reduction in children.

Group	No. of children	Initial examination		12 mo later		Reduction (%)	
		No. of noncarious teeth	Decayed, missing, or filled surfaces	Newly decayed, missing, or filled teeth*	Newly decayed, missing, or filled surfaces*	Teeth	Surfaces
NaF	397	5569	1869	245	281		
SnClF	394	5407	1846	32	46	86.9	83.5

* Compared with initial noncarious teeth or surfaces.

the initial examination. The children in the sodium fluoride group in this study had an average increase of 0.708 newly decayed, missing, or filled surfaces; and if this represents a reduction of approximately 40 percent in new decay, as previously reported by many other workers (*8*), then it is reasonable to suppose that a nontreated control group would have had 1.180 newly decayed, missing, or filled surfaces. Therefore, using the average increase in newly decayed, missing, or filled surfaces in the stannous chlorofluoride group (0.117), a reduction of 90 percent in dental caries is found when compared with children who did not receive fluoride therapy. These data strongly suggest that this new fluoride is superior to sodium fluoride in preventing new dental caries when used as a topical agent. Through the use of this compound, a greater reduction in dental decay may be expected for the children who do not receive the benefits of water fluoridation.

In the study begun in 1951, stannous fluoride was used as a topical agent, and children receiving it experienced greater protection than controls given sodium fluoride furnishing twice as much fluorine (*9*). This fact, together with the data reported here, suggests that the cation, tin, may influence the effectiveness of the fluorine and that additional studies should be made to find still more effective compounds.

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Reduction of Serum Lipides and Lipoproteins by Ethionine Feeding in the Dog

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A previous report from this laboratory dealt with the induction of fatty livers in rats by the administration of ethionine and related compounds(*1*). The observation of Farber and his associates (*2, 3*) that fat accumulated rapidly in the livers of fasted female rats after injection of DL-ethionine was confirmed. It was shown, in addition, that the L-isomer is also active. In order to determine the structural specificity of this action of ethionine, the following compounds were tested for their fatty-liver-inducing action: ethionine sulfoxide, S-propylhomocysteine, S-isopropylhomocysteine and S-ethylcysteine. Only ethionine sulfoxide was found active.

The effects of ethionine administration on serum lipides of the dog are described here (*4*). It is shown that, in addition to inducing fatty livers (*5*), prolonged oral administration of ethionine results in an almost complete disappearance of circulating lipides, which are restored to normal levels upon removal of ethionine from the diet.

The dogs used in this experiment had been fed a daily diet containing 30 g of lean meat and 3 g of sucrose per kilogram of body weight, 2 g of bone ash, 3 ml of fish oil containing 1200 AOAC units of vitamin D and 3000 units of vitamin A, one tablet containing a vitamin mixture (*6*) and another tablet containing a salt mixture (*7*). Along with the diet, 125 mg of DL-ethionine was fed daily in the form of a tablet. With few exceptions, the dogs ate well during the period of observation. When a dog lost appetite as a result of ethionine feeding, force-feeding was resorted to.

Low-density, serum lipoproteins were determined by ultracentrifuging according to the method of de Lalla and Gofman (*8*). High-density lipoproteins were divided into two fractions in which the concentrations of lipoproteins less dense than 1.125 (L) and 1.20

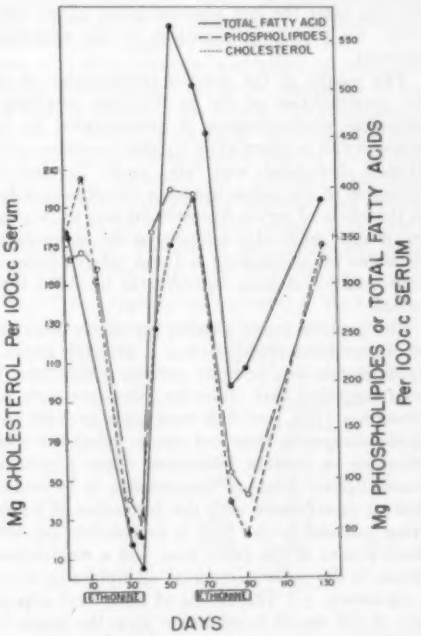

Fig. 1. Effect of ethionine feeding on concentrations of total fatty acids, phospholipides, and cholesterol of dog serum.

(L + T) were determined. The low-density lipoproteins were divided into four groups, Standard Sf 0–12, Standard Sf 12–20, Standard Sf 20–100, and Standard Sf 100–400, according to the system recently adopted by Gofman (*8*). The term *Standard Sf* signifies that the flotation rate has been determined under specified conditions in a solution of density 1.063 and that the concentrations in milligram percent have been corrected for the effects of concentration on flotation rate.

Aliquots of serum were analyzed for total fatty acids, total cholesterol, and lipide phosphorus, according to methods previously published (*9–11*).

Twelve dogs were used in this study, and typical results obtained with dog 110 are shown in Figs. 1 and 2. The total period of observation was 130 days, and during that time ethionine was fed from the 9th to the 36th day and from the 65th to the 90th day. The daily feeding of 125 mg of ethionine resulted in a pronounced fall in the concentration of all lipidé constituents of the serum. When the feedings of ethionine were discontinued, the levels of all lipide constituents in serum promptly returned to normal.

The four groups of low-density lipoproteins decreased during the ethionine administration. The distinction between the high-density L-lipoproteins and the high-density T-lipoproteins is not so clearly defined in dogs as it is in human beings. Both, however, shared in the decrease, and both returned to normal upon withdrawal of ethionine from the diet.

The tissues of two dogs were examined histologically 65 days after the last administration of the ethionine (*12*). No damage attributable to the ethionine was detected.

The results of the present investigation show that the accumulation of fat in the liver resulting from ethionine administration is accompanied by a pronounced fall in circulating lipides, involving phospholipides, cholesterol, and fatty acids. In view of the reduction of the serum lipides, a simultaneous decrease in the levels of serum lipoproteins was to be expected, but it is of particular interest, in this connection, that ethionine administration reduced all fractions of the high- and low-density lipoproteins to about the same extent.

The question arises whether the effects observed here on lipoproteins resulted from a primary action upon lipide metabolism or upon protein metabolism. It has been suggested that ethionine interferes with protein formation (*13*), and it is reasonable to infer that the lipide changes in liver and serum reflect the action of ethionine on protein formation. Since practically all serum lipides exist as lipoproteins, it is conceivable that an interference with the formation of lipide-carrying proteins in the liver is responsible for both the development of the fatty liver and a concomitant decrease in the concentration of all lipides in serum.

Summary. (i) The effects of daily oral administration of 125 mg of DL-ethionine upon the serum lipides and lipoproteins of dogs were studied. (ii) The feeding of the ethionine resulted in a prompt reduction in the levels of serum fatty acids, phospholipides, and cholesterol. At the end of 25 days, negligible amounts of these lipides remained in serum. (iii) A reduction in the levels of low- and high-density lipoproteins also resulted from the feeding of ethionine. In general, the extent of reduction in all lipoprotein fractions paralleled that observed in lipides. (iv) The removal of ethionine from the diet led to a prompt restoration of the concentrations of all lipide and lipoprotein constituents to normal.

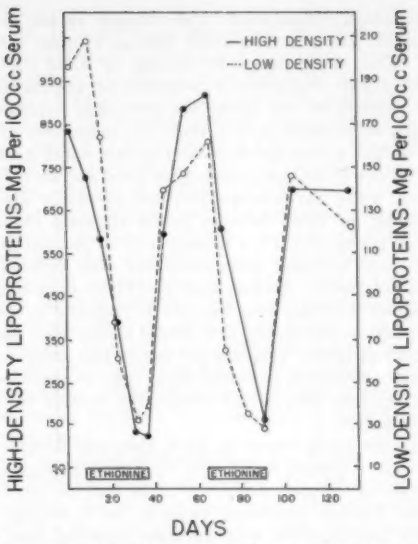

Fig. 2. Effect of ethionine feeding on concentrations of high-density and low-density lipoproteins of dog serum.

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7. Each salt tablet contained 600 mg NaCl, 450 mg magnesium citrate, 200 mg KH_2PO_4, 150 mg $CaHPO_4 \cdot 2H_2O$, 30 mg ferric citrate, 115 mg KCl, and 0.1 mg KI.
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Adrenal Cortex, Lipid Metabolism, and Atherosclerosis: Experimental Studies in the Rabbit*

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Previously reported observations revealed elevations of serum lipid fractions in patients treated with prolonged courses and large doses of cortisone and/or corticotropin (*1–3*). Not infrequently the serums of these patients had a milky (opaque) appearance. These observations have been extended to experimental animals (*4–6*).

Of a group of 150 rabbits on a diet of Purina chow that received cortisone acetate, hydrocortisone acetate, or corticotropin, 41 survived for 10 days or longer. The effect of the hormones on the plasma lipid partition is presented in rows 2–4, Table 1. The greatest alteration occurred in the neutral fat fraction. The most opaque plasmas contained the highest levels of neutral fat. The changes in total and esterified plasma cholesterol and of phospholipid were less pronounced than those of neutral fat.

These studies were extended to the cholesterol-fed rabbit. The technique of administering pure cholesterol to the rabbit without using fat solvents or stomach tube, and the effects of cholesterol feeding on the plasma lipid partition of normal young rabbits have been reported (*7*). These data are summarized in row 5, Table 1. The results of cholesterol feeding combined with daily injections of cortisone acetate, hydrocortisone acetate, or corticotropin are presented in rows 6–8, Table 1.

It is evident that the combination of cortisone or hydrocortisone injections with cholesterol feeding results in considerable enhancement of the elevations of all plasma lipid fractions observed with cholesterol feeding alone. Serum cholesterol levels as high as 5050 mg/100 ml were occasionally observed, which, to our knowledge, have not been produced previously by any experimental procedure. Discontinuation of corticosteroid administration but continuation of cholesterol feeding was followed by a return of the plasma lipids to levels characteristic for cholesterol feeding alone. However, when corticotropin injections were combined with cholesterol feeding, no significant enhancement was observed.

In all the rabbits, careful pathological studies were performed. After 1 mo of cholesterol feeding, the rabbits developed definite signs of atherosclerosis of the ascending aorta, of the arch, of the mitral and/or aortic valve, and only occasionally of the pulmonary and coronary arteries. After 3 to 4 mo, large, confluent plaques covered the ascending and descending aorta, the aortic and mitral valves, the coronary and pulmonary arteries. In addition, lipidosis of spleen, kidneys, joints, and skin was frequently present. Animals subjected to cortisone or hydrocortisone injections in addition to the cholesterol feeding exhibited, at comparable time intervals, marked inhibition of atherogenesis and delayed deposition of cholesterol in the tissues when compared with those treated with cholesterol alone.

Recently Seifter *et al.* (*8*) noted, in cholesterol-fed rabbits injected with hyaluronidase, enhancement of atherogenesis, despite lower plasma cholesterol levels; these effects were attributed to increased tissue permeability. Our studies suggest that corticosteroids diminish tissue permeability and that their administration results in diminished atherogenesis, despite higher plasma cholesterol levels. Additional studies utilizing combinations of cholesterol, corticosteroids, and hyaluronidase support this concept (*9*).

In summary then, cortisone and hydrocortisone produce significant, although moderate, elevations of the plasma lipid fractions in the rabbit. The combination of cholesterol feeding with daily injections of these hormones produces extreme elevations of all plasma lipid fractions, especially of plasma cholesterol. Nevertheless, atherogenesis and deposition of cholesterol in other tissues, in the latter group, is definitely depressed, possibly because of the diminished tissue permeability produced by these hormones.

Table 1. Average maximal changes in plasma lipids observed with different regimens of treatment in the rabbit.

	No. of animals	Cholesterol		Phospholipids		Neutral fats		Total lipids		Time (wk)
		(mg %)	Times normal	(mg %)	Times normal	(mg %)	Times normal	(mg %)	Times normal	
Control	119	49		103		198		350		
Corticotropin	15	95	1.9	150	1.5	337	1.7	582	1.7	5.5
Hydrocortisone	8	93	1.9	187	1.8	692	3.5	972	2.8	3
Cortisone	18	158	3.1	278	2.8	1019	5.0	1454	4.2	5
Cholesterol	28	1476	30.0	460	4.6	1094	5.5	3030	8.7	12
Cholesterol and corticotropin	4	877	17.9	423	4.2	955	4.8	2255	6.4	7
Cholesterol and hydrocortisone	4	1745	35.7	745	7.5	2260	11.3	4750	13.6	5
Cholesterol and cortisone	18	2079	42.5	890	8.9	1736	8.8	4705	13.4	9

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Primary Isolation and Propagation of Influenza Virus in Cultures of Human Embryonic Renal Tissue*

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A virus of the influenza-A type has been isolated directly from the nasal washings of a patient by single passage in cultures of human embryonic renal tissue and has been propagated by additional passages in cultures of this same tissue. The primary isolation of influenza virus by tissue culture from which hemagglutinins can be demonstrated and utilized for serological identification of the virus has not been previously reported, nor has growth of influenza virus been demonstrated in cultures of human tissue. Moreover, this use of human tissue culture provides an opportunity to study the characteristics of influenza virus without the necessity of passage through cells of another host species.

Kidneys from a 25-cm human embryo obtained following a spontaneous abortion were preserved as small fragments, 1 to 2 mm in diameter, in Hanks-Simms solution (*1*) for 13 days at 4°C prior to preparation of the cultures; 15 to 20 fragments were planted on the walls of 50-ml glass tubes that had been preheated to 45°C (*2*). To each tube was added 3 ml of nutrient medium: bovine amniotic fluid, 90 percent; bovine embryo extract, 5 percent; inactivated horse serum, 5 percent; phenol red 0.002 percent; penicillin, 200 units/ml, and streptomycin, 200 μg/ml (*3*). The cultures were incubated at 35°C in a horizontal stationary position, and nutrient fluids were replaced at weekly intervals. By the seventh day there was epithelial outgrowth from most of the fragments, and this had attained a diameter of 0.5 to 1.0 cm at 14 days. Each culture was inoculated at this time with 0.1 ml of nasal washing obtained from a patient in Jan. 1953. Nutrient fluids were replaced twice weekly following inoculation.

The presence of virus was determined by hemagglutination at room temperature both with 0.25 percent human type-O erythrocytes and pooled fowl erythrocytes and also by growth in subsequent tissue culture and in the amniotic sac of 10- to 11-day chick embryos. Hemagglutination-inhibition tests using human type-O erythrocytes were carried out with standard influenza virus-immune rooster antiserums and hemagglutinating antigen, strains PR8, FM1, FW-1-50 and Lee, obtained through the Biological Depot, Army Medical Service Graduate School, Walter Reed Army Medical Center, Washington, D.C. All antiserums were treated with receptor-destroying enzyme prepared by culture filtrates of the Inaba strain of *Vibrio cholerae*.

Table 1 shows the hemagglutination titers of tissue-culture fluids as determined by the addition of 0.25 percent human type-O erythrocytes. Although hemagglutinins could be detected earlier at the second tissue-culture passage, there was no increase in titer. The lack of hemagglutination by subsequent fluids was probably due to a paucity of additional susceptible cells for viral multiplication. Treatment of these fluids with receptor-destroying enzyme of *Vibrio cholerae* did not increase the hemagglutinating titers, although fresh nutrient mediums had sufficient nonspecific inhibitor to prevent hemagglutination of human type-O red blood cells by 16 hemagglutinating units of infectious PR8 virus after overnight incubation at 37°C. Infectivity titrations in the amniotic sac of the chick embryo demonstrated an increase from $10^{2.6}$ EID_{50} in the nasal washing to $10^{5.0}$ EID_{50} in the pooled third-day fluids from the second tissue-culture passage. It is likely that these titers were an index of the number of viral particles capable of adaptation to the chick embryo rather than a measure of the total infectious virus.

In no instance were hemagglutinins for fowl erythrocytes demonstrated in tissue-culture fluids. However, the initial nasal washing and each tissue-culture fluid shown in Table 1 upon single passage through the amniotic sac of the chick embryo yielded hemagglutinins for fowl erythrocytes. Inoculation of these same tissue-culture fluids in the allantoic sac of the chick embryo did not result in viral growth as measured by hemagglutination. The amount of virus inhibited by nonspecific inhibitor of hemagglutination

Table 1. Hemagglutination titers of fluids from individual tissue cultures, expressed as the reciprocal of final virus dilution. The four cultures *a*, *b*, *c*, *d* were inoculated with 0.1 ml of original nasal washing; at second passage four more cultures, *w*, *x*, *y*, *z*, were inoculated with 0.1 ml of the third-day fluid from culture *c*.

Day	First tissue culture passage				Second tissue-culture passage			
	a	*b*	*c*	*d*	*w*	*x*	*y*	*z*
0	0	0	0	0	0	0	0	0
3	0	0	64	0	128	32	32	64
7	0	32	8	32	0	0	0	0
10	0	0	0	0	0	0	0	0

Table 2. Comparison of human tissue culture and chick embryo adapted GL1134 influenza-A virus with other influenza-A and -B viruses by hemagglutination-inhibition.

Antiserum	Hemagglutination-inhibition titer, expressed as the reciprocal of the initial serum dilution					
	PR8	FM1	FW 1-50	Lee	GL1134 TC	GL1134 E5
PR8	3200				< 50	< 50
FM1		800			< 50	< 50
FW-1-50			800		200	200
Lee				800	< 50	< 50
GL1134 Acute	400	50	50	50	50	50
GL1134 Convalescent	400	200	200	50	400	100

in fresh bovine amniotic fluid increased eightfold after one passage through the amniotic sac of the chick embryo. Therefore the virus grown in human embryonic renal tissue was in the O phase (*4*).

Virus propagated in tissue culture was compared with the same virus that had been through five chick-embryo passages from the original nasal washing. The results of hemagglutination-inhibition with known influenza-A and -B antiserums are shown in Table 2, and it can be seen that this strain (GL1134A-53) is related to FW-1-50 influenza-A virus. Although convalescent serum inhibited hemagglutination by virus grown in tissue culture to a greater degree than that grown in the chick embryo, no assumptions should be made on the basis of this single serum, which was obtained 2 mo after the onset of illness.

Further studies on the growth of influenza viruses in cultures of human tissues, the characteristics of the virus, and the effects of multiplication on human cells are in progress.

Addendum. Since submission of this paper, additional strains of influenza-A and -B viruses have been isolated and propagated directly from nasal washings in both human embryonic lung and kidney tissue cultures.

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31 March 1954.

Communications

Lipogenesis by Cells of the Cornea

The capacity for neutral fat formation by nonadipose tissue is of possible relevance to the problems of fatty degeneration, atherosclerosis, and certain lipid histiocytoses. Simms *et al.* (*1–4*) have studied fat formation in chicken fibrocytes and concluded that serum contains lipoid soluble substances (called lipfanogens) that can be converted into fat.

The cornea is especially suitable for the study of such fat formation, since it is a relatively simple structure, is avascular, and contains no stainable fat. In a series of observations (*5*) on the cornea of the living rabbit and the incubated cornea, we have found that oleic acid and sodium oleate induce sudanophilic fat formation in all the cells of the cornea (epithelium, stroma, and endothelium) so long as serum is present. The experiments *in vivo* were made by injecting approximately 0.1 ml of oleic acid suspension or 10 percent sodium oleate solution into the corneal stroma. The experiments *in vitro* were made, for the most part, by incubating corneal buttons at 37°C in 2 ml of rabbit serum to which 2 drops of 10 percent sodium oleate were added. This technique was varied for specific purposes as will be evident in the conclusions.

Sudanophilic globules began to appear in the cytoplasm of the cells in approximately 6 hr and continued to increase in amount for at least 2 wk. This process appeared to be a true lipogenesis and was exclusively intracellular. Immersion of the corneal explants in 1 percent sodium fluoride or 1 percent potassium cyanide, or exposure of the buttons to 60°C for 1 hr prior to the incubation, completely blocked the lipogenesis. No effect was found, however, with similar heating of the serum prior to incubation. Variation of *p*H showed fat formation only in the range of 5.6–8.2 with maximal fat formation in 6.0–7.8. Serum was essential and could not be replaced by glucose-saline or glycerol-saline mediums.

The oleic acid or oleate salt appeared to be a specific and essential substrate. Of the other aliphatic acids tried unsuccessfully were elaidic acid, undecylenic acid, palmitic acid, arachidic acid, pelargonic acid, n-caproic acid, butyric acid, and acetic acid. Stearic acid resulted in a minimal fat formation (possibly attributable to contamination by oleic acid).

The lipogenesis did not result from contact with necrotizing agents other than oleic acid and sodium oleate. It did occur, however, abundantly with hydrolyzed rabbit fat and hydrolyzed olive oil.

Similar results were obtained with rabbit, beef, cat, and human corneas and with rabbit, horse, or human serum.

The fat formation occurred exclusively in viable cells. Those close to the site of oleic acid injection showed pycknotic degeneration but no sudanophilia. Although lipogenesis occurred equally in all the native cells of the cornea, none was found in the invading polymorphonuclear cells and only moderate amounts in the macrophages. Comparative studies on nonocular tissue are now under investigation.

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Toxicity of Sarin in Bullfrogs

The Chemical Corps has a continuing and necessary interest in studies concerned with the mechanism of action of "nerve gases," compounds that have a powerful anticholinesterase activity. A major part of the fund of knowledge concerning the fundamental physiology of nervous activity has been obtained through studies on poikilotherms, especially the frog. Consequently, data concerning the effect of anticholinesterase drugs on cold-blooded animals are directly related to Chemical Corps research.

Sarin (isopropyl methyl phosphonofluoridate) is a powerful anticholinesterase drug (*1*). Details of its pharmacology and toxicology in the mouse, rat, guinea pig, rabbit, cat, dog, sheep, goat, and monkey have been published by British investigators (*2*). This communication summarizes the toxicity of this compound for the bullfrog, *Rana catesbeiana*.

Frogs, weighing 400 to 500 g each, were injected with the drug, dissolved in amphibian saline, into the dorsal lymph sac. Controls received similar injections of plain amphibian saline. The frogs were then put into glass aquariums kept at 22°C and observed until death or for 3 days after injection. Table 1 gives the results. If the logarithm of the dose is plotted as a function of percentage dead for that dose, the LD_{50} is seen to be about 6 mg/kg body weight.

Table 1. Illustrating the toxicity of sarin to bullfrogs.

No. of frogs	Dose (mg/frog)	Results
6	0.060	No effect
6	.080	No effect
6	.100	No effect
5	.500	All alive and active 3 days later
17	1.000	1 dead
11	2.000	1 dead
6	4.000	4 dead
6	8.000	4 dead

It has recently been reported that sarin is the most toxic of three known compounds of the nerve-gas type (*3*). The toxic dose for man is estimated to be 0.7 to 7.00 mg (*3*). For a 70-kg man, this value would amount to 10 to 100 μg/kg to kill. Rabbits given 40 μg/kg of sarin intravenously stop breathing in about 10 sec (*2*). The blood pressure of anesthetized cats, given 200 μg/kg of sarin intravenously, is rapidly depressed to about 30 mm Hg. At such pressure the heart continues to beat effectively for several minutes after respiration ceases (*2*).

It is evident that the bullfrog is resistant to relatively large amounts of sarin given by injection. The only signs of poisoning noticed were observed in frogs given doses exceeding 1 mg. Such animals were partially anesthetized. They showed no spontaneous movements and responded sluggishly to tactile stimuli. The righting reflexes were present. After 24 hr these signs disappeared, and the frogs seemed to be normal. No blood or tissue cholinesterase values were estimated.

The explanation of the great resistance to, and surprising recovery from, sarin poisoning in bullfrogs is not certain. In mammals two key effects of such poisoning are paralysis of external respiration and depression of circulation. In frogs such effects merely anesthetize the animals until detoxification takes place. In addition, the functional integrity of frog nerves persists even at remarkably low cholinesterase levels (*4*).

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24 June 1954.

Morphologic Variation and Mode of Growth of Devonian Trepostomatous Bryozoa

Ramose fossil Bryozoa rarely are so situated in enclosing sediments that colonies can be assembled and studied in detail. The Hamilton group of Middle Devonian age in New York State contains colonies of at least three genera. Several have been restored and thin-sections made throughout their length.

The cortical, thick-walled portion of a colony (Fig. 1) contains diaphragms and other structures used in the classification of the order. The stage of development of the cortical region at any one level within the colony can be expected to control structural variations, at least of a quantitative nature. In the axial region of the colony the zooecia are thin-walled and diaphragms and other structures are rare.

Data commonly considered to be of value in dis-

crimination of species include the number of diaphragms, breadth of the cortical region, thickness of the zooecial walls, and the angle at which the zooecia reach the surface. These measurements are found to vary so widely within one colony that as many as three "species" can be designated from one end to the other.

The axial ratio (ratio of the diameter of the axial region to the diameter of the branch) was considered constant for any one species by G. W. Lee [*Mem. Geol. Survey G. Brit.* **1** (3), 135–195 (1912)] and subsequent workers. According to Lee, the proximal ends of the cortex were absorbed as the distal ends were extended. The rate of absorption was assumed to be balanced with the rate of growth, so that the axial ratio remained constant. The axial ratios in different parts of single colonies of the Hamilton group, however, show more variation than Lee allowed within species. On this basis also, as many as three "species" can be differentiated within a colony.

The present investigations resulted in an alternate hypothesis of the mode of growth of ramose colonies that is more consistent with axial ratio measurements and other observations. This new interpretation assumes resorption of the growing tips at the distal ends of the thick-walled regions. The cycle presumably began with growth of the zooecia in the thin-walled region so as to extend the growing tips of the colony. A thick-walled zone was then formed around the tips. Next, resorption from the outer ends of the zooecia back toward the base of the thick-walled region removed distal portions of walls and associated structures such as diaphragms. The amount of resorption varied greatly among species, but usually some traces of the thick-walled region remained. Another cycle began with the extension of the thin-walled region. This growth, in the distal ends of the colony, lengthened the branches.

Proximal to the growing tips of the colony, where the zooecia established their thick-walled regions in permanent positions opening along the sides of the branches, there are no signs of resorption. Zooecial growth was restricted to the cortex. Thickness of walls, number of diaphragms, and other intramural structures increase progressively toward the base of the colony. The thin-walled, axial region was not affected. Thus, changes in the axial ratio result from a slow proximal increase in the breadth of the cortex, with resulting increase in the diameter of the colony and no accompanying changes in the axial region.

A study of complete colonies indicates that a wider range of specific variation must be allowed in the structures that are controlled largely by the stage of development of the colonies.

RICHARD S. BOARDMAN

U.S. Geological Survey
Washington 25, D.C.

19 July 1954.

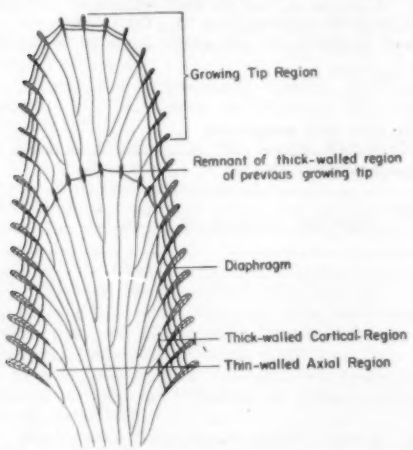

Fig. 1. Idealized diagram of a ramose bryozoan in axial view.

Chromosomes of *Hypomyces solani* f. *cucurbitae*

The cytology of *Hypomyces solani* f. *cucurbitae* was first investigated by Hirsch (*1, 2*). On the basis of her investigations she concluded that the haploid chromosome number is four in the hermaphroditic strain, three in the male, three in the female, and two in the neuter. When the hermaphrodite mutates to male, it loses one of its sex chromosomes; when it mutates to female it loses the other. Hirsch claimed that hermaphrodites and neuters, which are produced among the offspring of the cross ♀ × ♂ (*3*), arise as a result of occasional nondisjunction of sex chromosomes.

However, my genetic investigations (*4*) were not in accord with Hirsch's interpretations, and hence the cytology of *Hypomyces solani* f. *cucurbitae* required reinvestigation. It is the purpose of this paper to describe briefly the results of such reinvestigation (*5*).

By employing the aceto-orcein smear technique, which was used successfully by McClintock (*6*) on *Neurospora crassa*, it was possible to study the nuclear behavior in the ascus and to determine the number of chromosomes in each of the four strains. Priority was given to the cross ♀ × ♂, since the four sex strains can be obtained from such a mating, and hence the chromosome number in each strain would be determined. Careful analysis of diakinesis, prometaphase I, and metaphase I figures has revealed that the number of bivalents at these stages was consistently four. At early anaphase I and mid-anaphase I, eight dyads could be counted. During the following divisions each nucleus was observed to contain four chromosomes. Nondisjunction of what are called the two sex chromosomes, as reported by Hirsch to occur frequently during the first anaphase, has never been seen. Since, from the cross ♀ × ♂, the four sex strains are produced, and since all nuclei in the ascus at the same stage of division have the same number of chromosomes, it seems justifiable to conclude that the haploid chromosome number in hermaphrodite, female, male,

and neuter is four. Asci derived from the cross ♀ × ♂ were also studied cytologically, and the pairing behavior and chromosome number were found to be the same. A detailed report of these findings will be presented subsequently.

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References and Notes

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6. B. McClintock *Am. J. Botany* **32**, 671 (1945).

22 June 1954.

Instability of Compounds in the Folic Acid Series

There is currently a quickening of interest in studies that involve compounds in the folic acid series, particularly with regard to their effect in biological systems concerned with single-carbon transfer (*1–3*). The chemical manipulation of these compounds may result in their partial decomposition, especially under conditions where wide changes in *p*H are encountered and where the compounds are subjected to the vicissitudes of paper chromatography.

Exposure to air causes rapid oxidation of some of the folic acid compounds. Photolytic breakdown occurs when these compounds are exposed to light; this has been studied in some detail in the case of pteroylglutamic acid, but precise information is lacking with respect to other compounds in the series. Acid and alkaline conditions departing from the isoelectric point or the *p*H of formation of the compound cause various types of transformation. The citrovorum factor is rapidly converted by acid into imidazoline compounds (anhydroleucovorin-A and -B and isoleucovorin chloride), which may undergo further decomposition (*4*). These imidazoline compounds are interconvertible under various conditions of acidity and revert to leucovorin upon anaerobic treatment with alkali, while a similar aerobic treatment converts them to pteroylglutamic acid. The lability of aminopterin should be noted. This compound is readily deaminated by acid or alkali to form pteroylglutamic acid, with consequently an abrupt change in biological properties. The content of pteroylglutamic acid in aminopterin, which has been noted by various investigators (*5–7*), may be greatly augmented by inappropriate experimental manipulation. Similar comments apply to 4-amino-10-methylpteroylglutamic acid.

In planning experiments with the folic acid series of compounds, it may be well to refer to the original literature for a description of their properties. A qualitative summary of these properties together with references for additional use appears in Table 1.

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27 July 1954.

Table 1. Some properties of the folic acid compounds.

Substance	Destruction caused by				References
	Light	Atmospheric oxygen	Low *p*H	High *p*H	
Pteroylglutamic acid (PGA)	+	±	+	±	(*8*) (*9*)
Tetrahydro-PGA		+++			(*10*) (*11*)
10-formyl-PGA				++	(*11*) (*12*)
10-formyl-tetrahydro PGA		+++		+++	(*4*) (*11*)
5-formyl-tetrahydro PGA (leucovorin)		-	+++	-	(*4*) (*11*) (*12*) (*13*)
Anhydroleucovorin-A		-	+	+++	(*4*)
Anhydroleucovorin-B			+	+++	(*4*)
Isoleucovorin chloride		-	-	+++	(*4*)
4-amino-PGA (aminopterin)	+	±	+	++	(*14*) (*15*)

Meetings & Conferences

September

8–9. Soc. of General Physiologists, annual, Woods Hole, Mass. (J. B. Buck, National Institutes of Health, Bethesda 14, Md.)

8–10. American Physiological Soc., Madison, Wis. (W. B. Youmans, Dept. of Physiology, Univ. of Wisconsin, Madison.)

8–10. American Soc. of Mechanical Engineers, fall, Milwaukee, Wis. (O. B. Schier, II, 29 W. 39 St., New York 18.)

8–10. American Sociological Soc., Urbana, Ill. (J. W. Riley, Jr., A.S. Soc., New York Univ., New York 3.)

9–11. American Political Science Assoc., annual, Chicago, Ill. (J. Gange, 1785 Massachusetts Ave., NW, Washington 6, D.C.)

9–17. International Cong. of Ophthalmology, 17th, Montreal, Canada, and New York, N.Y. (W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn.)

10–12. Gerontological Soc., Gainesville, Fla. (A. J. Carlson, Univ. of Chicago, Chicago 37.)

10–13. Econometric Soc., Montreal, Canada. (R. L. Cardwell, Cowles Commission, Univ. of Chicago, Chicago 37.)

10–15. Inst. of Mathematical Statistics, American Statistical Assoc., and Econometric Soc., Montreal, Canada. (K. J. Arnold, Dept. of Mathematics, Michigan State College, East Lansing.)

10–16. International Symposium on Problems in Contemporary Optics, Florence, Italy. (S. S. Ballard, The Rand Corp., Santa Monica, Calif.)

11–19. International Cong. of Industrial Chemistry, 27th, Brussels, Belgium. (Mr. Guilmot, 32 Rue Joseph II, Brussels.)

12–16. American Inst. of Chemical Engineers, Glenwood Springs, Colo. (C. H. Prien, Research Inst., Univ. of Denver, Denver 10, Colo.)

12–17. American Chemical Soc., annual, New York City. (R. M. Warren, 1155 16 St., NW, Washington 6, D.C.)

12–17. International Assoc. for the Prevention of Blindness, New York City. (Prof. Franceschetti, 3 Ave. Miremont, Geneva, Switzerland.)

12–17. International Cong. of Cardiology, Washington, D.C. (L. W. Gorham, American Heart Assoc., 44 E. 23 St., New York 10.)

12–17. International Organization Against Trachoma, Montreal, Can. (A. Sorsby, 45 Lincoln's Inn Field, London W.C.2.)

13–14. American Microscopical Soc., annual, Philadelphia, Pa. (C. J. D. Brown, Dept. of Zoology and Entomology, Montana State College, Bozeman.)

13–15. Analytical Instrument Clinic, 3rd annual, Philadelphia, Pa. (A. H. Peterson, 4400 5 Ave., Pittsburgh 13, Pa.)

13–17. Illuminating Engineering Soc., Atlantic City, N.J. (A. D. Hinckley, 1860 Broadway, New York 23.)

13–17. Assoc. of Applied Biologists, 50th anniversary, London, Eng. (R. K. S. Wood, Imperial College of Science and Technology, London, S.W.7.)

13–18. International Cong. of Nutrition, 3rd, Amsterdam, Netherlands. (M. van Eekelen, 61 Catharynesingel, Utrecht, Netherlands.)

13–19. International Cong. on Industrial Medicine, 11th, Naples, Italy. (Sec. of Cong., Istituto Medicine del Lavoro, Universita, Policlinico, Piazza Miraglia, Naples.)

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September, *contd.*

13–19. International Soc. of Blood Transfusion, 5th, Paris, France. (Col. Julliard, 57 Boulevard d'Auteuil, Boulogne sur Seine, France.)

13–20. International Soc. of the History of Medicine, 14th, Rome and Salerno, Italy. (M. Galeazzi, Citta Universitaria, Rome.)

13–25. International Instrument Cong. and Exposition, 1st, Philadelphia, Pa. (R. Rimbach, 921 Ridge Ave., Pittsburgh 12, Pa.)

15–17. American Assoc. of Clinical Chemists, 6th annual, New York City. (M. M. Friedman, Lebanon Hospital, New York 57.)

15–18. International Cong. of Internal Medicine, 3rd, Stockholm, Sweden. (A. Kristenson, Karolinska Sjukhuset, Stockholm 60.)

15–29. International Union of Geodesy and Geophysics, Rome, Italy. (W. E. Smith, 1530 P St., NW, Washington 5, D.C.)

16–17. American Soc. of Photogrammetry, Philadelphia, Pa. (C. E. Palmer, 1000 11 St., NW, Washington 1, D.C.)

17–18. Calorimetry Conf., 9th annual, Schenectady, N.Y. (W. De Sorbo, GE Research Laboratories, Schenectady.)

19–24. American Acad. of Ophthalmology and Otolaryngology, New York City. (W. L. Benedict, 100 First Ave., Bldg., Rochester, Minn.)

21–23. Soc. for Experimental Stress Analysis, Philadelphia. (W. M. Murray, Central Square Station, P.O. Box 168, Cambridge 39, Mass.)

21–24. American Roentgen Ray Soc., Washington, D.C. (B. R. Young, Germantown Hospital, Philadelphia 44.)

22–24. Conf. on the Protection of Plants in Hot Climates, Marseilles, France. (P. Bonnet, Palais de la Bourse, Marseilles.)

22–24. Mississippi Valley Medical Soc., 18th annual, Chicago, Ill. (H. Swanberg, 209–224 W.C.U. Bldg., Quincy, Ill.)

22–28. International Symposium on High-Speed Photography and Kinematography, 2nd, Paris, France. (P. Naslin, Laboratoire Central de l'Armement, Fort de Montrouge, Arcueil, France.)

23–28. European Cong. and Clinical Chemistry, 1st, Amsterdam, Netherlands. (Ir. O. Meulemans, Racinelaan 17, Utrecht, Netherlands.)

24. American Medical Writers Assoc. 11th annual, Chicago, Ill. (H. Swanberg, Drawer 110, Quincy, Ill.)

24–25. International Symposium on Problems in Physiology and Pathology of the Eye, Iowa City, Iowa. (F. C. Blodi, Dept. of Ophthalmology, State Univ. of Iowa, Iowa City.)

24–27. International Soc. of Medical Hydrology, Vichy, Paris, and Enghien, France. (Dr. Francon, 55 Rue des Mathurins, Paris 8.)

26. Cong. of International Soc. of Medical Hydrology, Vichy and Paris, France. (G. Ammirandoli, Via Della Torretta 11, Montecatini Terme, Italy.)

26–2. International Union Against Tuberculosis, 13th, Madrid, Spain. (J. Aliz, Calle Francisco Silvela 20, Madrid.)

26–2. World Medical Assoc., 8th general assembly, Rome, Italy. (L. H. Bauer, 345 E. 46 St., New York 17.)

27–2. Interantional Conf. on Engineering Education, 2nd, Switzerland. (L. A. Rose, Univ. of Illinois, Urbana.)

27–2. Symposium on Macromolecular Chemistry, Turin and Milan, Italy. (A. Nasini, Corso Massimo d'Azeglio 48, Turin.)

October

1–5. International Cong. of Chronometry, Paris. (R. Baillaud, Observatoire National, Besançon, France.)

1–5. IRE Professional Group on Nuclear Science, annual, Chicago, Ill. (S. J. Goslovich, 517 Forest Ave., Glen Ellyn, Ill.)

2–6. International Cong. on Diseases of the Chest, 3rd, Barcelona. (American College of Chest Physicians, 112 E. Chestnut St., Chicago 2.)

3–5. Southern Psychiatric Assoc., Louisville, Ky. (G. Southerland, 2218 N. Charles St., Baltimore.)

3–6. World Medical Cong. of Homeopathy, 1st, Rio de Janeiro, Brazil. (R. Seidel, 1801 Porter St., Philadelphia, Pa.)

3–7. Electrochemical Soc., autumn, Boston. (H. B. Linford, Columbia University, New York 27.)

4–6. National Electronic Cong., 10th annual, Chicago. (K. Kramer, 852 E. 83 St., Chicago 19.)

4–7. International Plastics Cong., 6th, Turin, Italy. (M. Muzzoli, Salone Internazionale della Tecnica, 20 Via Massena, Turin.)

4–13. International Telecommunication Union, 17th, Geneva, Switzerland. (Sec., ITU, Palais Wilson, Geneva.)

5–7. American Inst. of Electrical Engineers, Middle Eastern District, Reading, Pa. (H. H. Henline, 33 W. 39 St., New York 18.)

5–8. International Cong. of Hydatid Diseases, 5th, Madrid. (J. C. Melendro, Hospital Provincial, Sorea, Spain.)

5–14. Conf. on Weights and Measures, 10th, Sèvres, France. (Sec., Bureau International des Poids & Mesures, Pavillon de Breteuil, Sèvres.)

6–7. Inst. of Radio Engineers, Professional Group on Nuclear Science, 1st annual, Chicago. (T. Fields, V.A. Hospital, Hines, Ill.)

7–8. Commercial Chemical Development Assoc., annual fall, Bedford, Pa. (W. T. Hack, Ethyl Corp., 100 Park Ave., New York 17.)

7–9. Pan American Homeopathic Medical Cong., 25th, Rio de Janeiro, Brazil. (H. O. Skinner, 2134 Grand Ave., St. Paul 5, Minn.)

7–22. Pan American Sanitary Cong., Santiago, Chile. (M. E. Bustamante, Pan American Sanitary Bureau, Washington 6, D.C.)

8–9. Acad. of Psychosomatic Medicine, 1st annual, New York City. (E. A. Brown, 75 Bay State Rd., Boston 15.)

11–12. Ferrimagnetism Conf., Silver Spring, Md. (L. R. Maxwell, U.S. Naval Ordnance Laboratory, Silver Spring.)

11–13. American Oil Chemists' Soc., 28th annual fall, Minneapolis. (L. R. Hawkins, AOCS, 35 E. Wacker Dr., Chicago 1.)

11–14. Cong. of International Anesthesia Research Soc., Los Angeles. (T. H. Sheldon, 102–110 Second Ave., Rochester, Minn.)

11–15. American Public Health Assoc., Buffalo, N.Y. (R. M. Atwater, 1790 Broadway, New York 19.)

11–16. Symposium on Light Microscopy and Symposium on Electron Microscopy, Highland Park, Ill. (W. C. McCrone, Illinois Inst. of Technology, Chicago 16.)

13–17. Audio Engineering Soc., annual, New York City. (C. J. LeBel, AES, P.O. Box 12, Old Chelsea Station, New York 11.)

14–15. Bicentennial Conf. of the Columbia University College of Pharmacy, New York City. (G. W. Merck, Merck & Co., Rahway, N.J.)

14–16. Electron Microscope Soc. of America, Highland Park, Ill. (J. R. Cooper, ESMA, General Electric Co., Cleveland 12, Ohio.)

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14–16. Gaseous Electronics Conf., 7th annual, New York, N.Y. (L. H. Fisher, New York University, New York 53.)

14–16. Indiana Acad. of Science, Lafayette, Ind. (W. A. Daily, Eli Lilly & Co., 740 S. Alabama St., Indianapolis 6.)

14–16. Optical Soc. of America, annual, Los Angeles. (A. C. Hardy, Massachusetts Institute of Technology, Cambridge 39, Mass.)

15–17. International Colloquium on Dermatology and Syphilography, 5th, Marseilles, France. (J. Bonnet, Hotel-Dieu, Place Daviel, Marseilles.)

18–20. Conf. on Electrical Insulation, Pocono Manor, Pa. (A. McLean, 2101 Constitution Ave., Washington 25, D.C.)

18–20. IRE–RETMA, fall, Syracuse, N.Y. (E. K. Gannett, 1 E. 79 St., New York 21.)

18–21. Mental Hospital Inst., 6th, Minneapolis, Minn. (W. Malamud, 80 E. Concord St., Boston 18.)

18–22. American Soc. of Civil Engineers, New York City. (W. M. Carey, 33 W. 39 St., New York 18.)

18–22. Soc. of Motion Picture and Television Engineers, semi-annual, Los Angeles. (SMPTE, 342 Madison Ave., New York 16.)

19. American Soc. of Safety Engineers, Chicago. (J. B. Johnson, 425 N. Michigan Ave., Chicago 11.)

21–22. National Noise Abatement Symposium, 5th annual, Chicago. (S. M. Potter, Illinois Inst. of Technology, Chicago 16.)

21–23. International Assoc. of Milk and Food Sanitarians, Atlantic City, N.J. (H. L. Thommasson, IAMFS, Box 437, Shelbyville, Ind.)

21–23. International Symposium on the Dynamics of Virus Infections, Detroit. (Henry Ford Hospital, 2799 W. Grand Blvd., Detroit 2.)

21–24. American Dietetic Assoc., annual Philadelphia. (E. A. Atkinson, 620 N. Michigan Ave., Chicago 11.)

22. Symposium on the Nutritional Aspects of Blood Formation, Cincinnati, Ohio. (National Vitamin Foundation, 15 E. 58 St., New York 22.)

22–26. Symposium on Wind and Solar Energy, New Delhi, India. (UNESCO, 19 Ave. Kléber, Paris 16.)

24–27. Soc. of American Foresters, Milwaukee. (H. Clepper, 425 Mills Bldg., Washington 6, D.C.)

25–27. Assoc. of American Medical Colleges, Bedford Springs, Pa. (AAMC, 5 S. Wabash Ave., Chicago 3.)

25–30. International Cong. of Odontology, 1st, São Paulo, Brazil. (F. Degni, Rua Marconi 131, São Paulo.)

26. Assoc. of Consulting Chemists and Chemical Engineers, annual, New York City. (A. B. Bowers, 50 E. 41 St., New York 17.)

27–28. Conf. on Plastics in Building, Washington, D.C. (Building Research Inst., 2101 Constitution Ave., Washington 25.)

27–29. International Symposium on the Hypophyseal Growth Hormone, Its Nature and Actions, Detroit, Mich. (R. W. Smith, Henry Ford Hospital, Detroit 2.)

28–30. American Soc. for Aesthetics, Bloomington, Ind. (R. R. Patrick, Cleveland Museum of Art, Cleveland 6, Ohio.)

28–30. International Symposium on Temperature, Washington, D.C. (W. Waterfall, 57 E. 55 St., New York 22.)

31–1. American Soc. for the Study of Arteriosclerosis, annual, Chicago. (A. C. Corcoran, Cleveland Clinic, Cleveland 6, Ohio.)

November

1–3. Entomological Societies of Canada and Ontario, annual, Sault Ste. Marie, Canada. (R. H. Wigmore, Science Service Bldg., Ottawa.)

1–3. Geological Soc. of America, annual, Los Angeles, Calif. (H. R. Aldrich, 419 W. 117 St., New York 27.)

1–3. Paleontological Soc., annual, Los Angeles, Calif. (K. E. Caster, Dept. of Geology, Univ. of Cincinnati, Cincinnati 21, O.)

1–5. National Metal Cong., Chicago, Ill. (C. L. Wells, 7301 Euclid Ave., Cleveland, O.)

3–5. American Crystallographic Assoc., and 12th annual Pittsburgh Diffraction Cong., Pittsburgh, Pa. (P. K. Koh, Allegheny Ludlum Research Laboratories, Alabama Ave., Brackenridge, Pa.)

3–5. Soc. of Rheology, Washington, D.C. (W. R. Willets, Titanium Pigment Corp., 99 Hudson St., New York 13.)

3–6. American Soc. of Parasitologists, Memphis, Tenn. (A. C. Walton, Dept. of Biology, Knox College, Galesburg, Ill.)

3–6. American Soc. of Tropical Medicine and Hygiene, Memphis, Tenn. (J. E. Larsh, Jr., School of Public Health, Univ. of North Carolina, Chapel Hill.)

4–6. American Acad. of Tropical Medicine, Memphis, Tenn. (E. H. Hinman, Univ. of Puerto Rico School of Medicine, San Juan 22.)

6. Committee for the Scientific Study of Religion, fall, Cambridge, Mass. (R. V. McCann, 48 Mt. Auburn St., Cambridge.)

7. American College of Dentists, Miami, Fla. (O. W. Brandhorst, 4221 Lindell Blvd., St. Louis, Mo.)

8–11. American Dental Assoc., annual, Miami, Fla. (H. Hillenbrand, 222 E. Superior St., Chicago 11, Ill.)

8–11. American Petroleum Inst., 34th annual, Chicago, Ill. (API, 50 W. 50 St., New York 20.)

8–11. Southern Soc. of Cancer Cytology, annual, St. Louis, Mo. (J. E. Ayre, 1155 N. W. 14 St., Miami, Fla.)

8–12. American Soc. of Agronomy, annual, St. Paul, Minn. (L. G. Monthey, 2702 Monroe St., Madison 5, Wis.)

8–12. Soil Conservation Soc. of America, St. Paul, Minn. (H. W. Pritchard, 1016 Paramount Bldg., Des Moines, Iowa.)

10–11. Conf. on Electrical Techniques in Medicine and Biology, Chicago, Ill. (E. D. Trout 4855 Electric Ave., Milwaukee, Wis.)

11–12. Corrosion Cong., Frankfurt, Germany. (DECHEMA, Frankfurt a.M., W. 13.)

12–13. Inter-Society Cytology Council, Boston, Mass. (P. F. Fletcher, 634 N. Grand Blvd., St. Louis 3, Mo.)

12–Dec. 11. United Nations Educational, Scientific, and Cultural Organization, Montevideo, Uruguay. (UNESCO, 19 Ave. Kléber, Paris 16.)

15–17. National Conf. on Standards, 5th, New York City. (D. E. Denton, 70 E. 45 St., New York 17.)

17–19. American Meteorological Soc., Miami Beach, Fla. (K. C. Spengler, 3 Joy St., Boston 8, Mass.)

18–20. Acoustical Soc. of America, semiannual, Austin, Tex. (W. Waterfall, 57 E. 55 St., New York 22.)

18–20. Symposium on Precision Electrical Measurements, Teddington, Eng. (Director, National Physical Laboratory, Teddington, Middlesex, Eng.)

19–30. International Cong. of Civil Engineers, 2nd, Caracas, Venezuela. (L. B. Diaz, Av. Principal de los Caobos, Apartado 2006, Caracas.)

26–27. American Physical Soc., Chicago, Ill. (K. K. Darrow, Columbia Univ., New York 27.)

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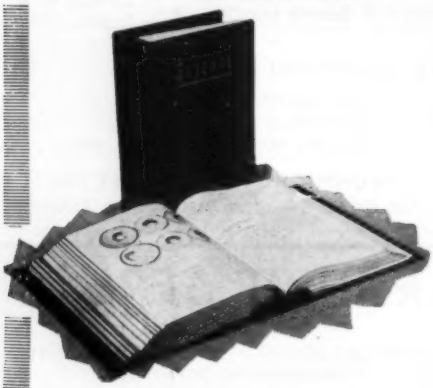

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